UDPR

Utah Diabetes Practice Recommendations
Diabetes Management for Adults

UTAH DEPARTMENT OF
HEALTH
Diabetes Prevention & Control Program

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Introduction

The Utah Diabetes Prevention and Control Program (DPCP) recognizes the importance of optimizing care for patients with diabetes. In promoting this objective, the DPCP organized a panel of interested health care professionals to develop the Utah Diabetes Practice Recommendations for Adults 2012 (UDPR). The recommendations are intended to foster current diabetes care practices, and to provide useful outlines to guide health care professionals in the screening, diagnosing, and appropriate management of people with diabetes. The materials in the UDPR build upon and complement national and regional diabetes protocols. Members of the UDPR Panel have identified decision points to assist clinicians in providing consistent and appropriate diabetes care for their patients.

This edition of the UDPR aims to draw attention not only to glycemic control, but to all the other factors that affect the health of your patient with diabetes. Hypertension control and lipid control are critical to the prevention of cardiovascular events and deaths, as well as renal and retinal disease. Randomized, controlled trials show that control of these three factors can reduce morbidity and mortality by 50% (Gaede et al., 2008).

Included in these recommendations are tools to support you in achieving safe glycemic control in your patients. Well-designed and effectively carried out studies such as the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS) have demonstrated convincingly that blood glucose control significantly affects the development of complications in individuals with either type 1 or type 2 diabetes. A direct link between blood glucose levels and the risk of complications has been firmly established, despite the fact that other factors such as genetics also play a significant role.

Providers should encourage individuals with diabetes to aim for the lowest blood glucose levels that do not place them at undue risk for hypoglycemia. The studies also show that any improvement in glucose control has the effect of slowing both the development and progression of microvascular complications.

NOTE: Guidelines should be used as instruments to assist providers in clinical practice. The practice standards introduced in the UDPR are based on published literature (evidence) and clinical opinion (consensus).

The position statement achieved through these guidelines may need to be modified when new evidence becomes available. Providers following these guidelines should be aware of ongoing developments in the field, evaluate their merits based on the level of evidence, and incorporate these results into their practice using their best clinical judgment.

Reference

Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008; 358(6): 580-591.

Summary of 2012 Updates

Diabetes care is an ever-evolving field and the members of the UDPR Panel strive to keep all information and recommendations current according to the most recent and accepted studies and findings. To provide the best available information, the UDPR are based on the American Diabetes Association Standards of Medical Care in Diabetes, current clinical best practices, and international and national studies that are widely accepted by diabetes professionals.

In this edition of the UDPR for Adults, the following updates have been added:

- **Diabetes Screening Protocol**

    In the 2011 edition of the Standards of Medical Care in Diabetes, hemoglobin A1c (A1C), if measured by a certified lab following Diabetes Control and Complication Trial (DCCT) protocols, was added as a diagnostic tool. For 2012, the reliability of A1C as a screening test is being questioned in elderly patients, those with hemoglobinopathies and/or anemia, and some ethnic groups. Screening using this method may not be as reliable as a 2-hour glucose tolerance test (GTT).

- **Cardiovascular Disease:**
  Aspirin Therapy

    Aspirin therapy is recommended to be individualized based on a patient's risk of all forms of cardiovascular disease. Updated recommendations are incorporated in the 2012 edition.

  Hypertension Therapy

    The 2012 ADA guideline newly recommends administration of one or more antihypertensive agent(s) at bedtime. See the Cardiovascular section for details.

- **New Sections**

    This edition of the UDPR has been expanded to include sections on Depression and Diabetes and Vaccine Administration.

- **Medication Summary**

    Since the last edition of this UDPR, additional medications have been developed or changed to generic versions. These medications include:, Linagliptin (Tradjenta), Exenatide ER (Bydureon), Sitagliptin/Metformin XR (Janumet XR), Linagliptin/Metformin (Jentadueto). Pioglitazone (Actos) is now available in generic form and pramlintide is sold only as SymlinPen. Dosage regimens of medications commonly used in the treatment of diabetes are found in Appendix C.

- **New Tools**

    A variety of clinical and patient-education tools have been integrated into this document as embedded Web links and in the appendix. Resources for providers include chronic kidney disease assessment and treatment algorithms, referral forms for diabetic eye exams and tobacco cessation, and a comprehensive foot exam form. Patient handouts cover foot care, self-monitoring of blood glucose, and nutrition.

Summary of Key Treatment Targets

Measure/Test	Target	Frequency	Comment
A1C	<7.0%*	Test at least semi-annually	As low as possible without significant hypoglycemia. *A higher goal may be necessary for certain individuals from special populations. See page 8.
Blood Pressure	<130/80 mmHg	Check at each office visit	
LDL Cholesterol	<70-100 mg/dL (depending on presence of CVD)	Test at least annually	
HDL Cholesterol	Women: >50mg/dL Men: >40 mg/dL		
Triglycerides	<150 mg/dL		
Microalbumin/ Creatinine Ratio	<30 mg/g of creatinine	Test annually	If positive, repeat test one month later, up to 3 times. Use 2 out of 3 results for diagnosis.
Serum Creatinine	See comment	Annually	The serum creatinine should be used to estimate GFR; if <60 mL/min/1.73 m^2 more frequent testing is required. www.kidney.org/professionals/ kdoqi/gfr_calculator.cfm
Dilated Eye Exam	Normal	Annually	High-risk should be tested more frequently; low-risk may require less often.
Comprehensive Foot Exam	Identify level of risk	Annually	Visually inspect at every visit if significant vascular disease, foot deformities, or loss of protective sensation is present, or if identified as high-risk (see Appendix D).

Guidelines for Frequency of Lab Tests & Examinations

Clinic Visit	At least every 3 months for those who are not meeting LDL cholesterol, blood glucose, or blood pressure goals; on new therapy; on insulin therapy; or with evidence of progression of microvascular or macrovascular disease
	At least every 6 months for those who are meeting blood glucose and blood pressure goals, are not on new therapy, and do not have evidence of progression of microvascular or macrovascular disease
Hemoglobin A1c	Same as for clinic visit above
Blood Glucose	Patient self-monitoring blood glucose (SMBG) records are acceptable (Appendix I)
	If patient is not self-monitoring blood glucose, test when fasting at each clinic visit and correlate with A1C
Blood Pressure [1]	Check and record at every visit
Foot Exams [2]	Screen feet annually: foot inspection, 10g monofilament exam, and 1 of 3 other neurosensory tests (pp 31-32; Appendix D)
	If High Risk: Visually inspect at every visit
Dilated Eye Exam [3,4]	Annually for most patients with non-proliferative diabetic retinopathy (NPDR) or microaneurysms, biennially for patients in good control and with a normal exam with advice from an ophthalmologist or optometrist (see Appendix F)
Microalbumin/ Creatinine Ratio [4,5]	Annually for patients without chronic kidney disease diagnosis
Serum Creatinine	Annually, more often if chronic kidney disease diagnosis
Fasting Lipid Profile	Annually (non-fasting may be acceptable[6])
Influenza Vaccine	Annually
Pneumococcal Vaccine	See page 39
Self-management Education	1. Upon diagnosis 2. When there are significant changes in therapy, the patient is not meeting targets, for pre-pregnancy counseling, or newly-diagnosed gestational diabetes 3. Annually reassess need for education
Dental Exam	Every six months for preventive care
Tobacco Use	During each visit; advise quitting and refer to cessation services (see Appendix G)

1. See section on hypertension (pgs. 18-26)
2. Refer to "Feet Can Last a Lifetime" packet for additional foot screening information (www.ndep.nih.gov).
3. Exception: Examine when planning pregnancy if possible and in first trimester with close follow-up
4. Exception: Screen in first trimester in pregnancy
5. See section on nephropathy (pgs. 33-35)
6. van Dieren et al. Non-fasting lipids and risk of cardiovascular disease in patients with diabetes mellitus. *Diabetologia* 2011 Jan;54(1):73-7. Epub 2010 Oct 20.ReferenceDOI 10.1007/s00125-010-1945-z

Diabetes in Utah and the United States

Prevalence

Diabetes continues to be at the forefront of public health and clinical concerns. There were approximately 1.9 million new cases of diabetes diagnosed in the past year in the U.S. (Centers for Disease Control & Prevention, 2011). The most recent estimate shows that nearly 19 million Americans have been diagnosed with diabetes, and another 7 million are believed to have diabetes but have not yet been diagnosed. Findings from the Behavioral Risk Factor Surveillance System survey indicate that about 120,000 Utah adults, or 6.8 percent of the adult population in the state, have been diagnosed with diabetes (Utah BRFSS 2011). An estimated 45,000 more adults in the state have diabetes but are not diagnosed.

Complications

Diabetes is associated with a number of serious and potentially fatal complications. It is estimated that **two out of three individuals with diabetes die prematurely from heart disease or stroke**. Diabetes is thought to be responsible for about half of all new cases of end-stage renal disease requiring **dialysis**, and is the leading **cause of blindness** among working age adults. Over half of all non-traumatic **lower extremity amputations** are related to complications of diabetes. Tobacco use worsens each of these complications.

Cost

Diabetes is a common, and potentially disabling, chronic disease that costs Americans over $174 billion a year. **One out of every five health care dollars is spent on treating diabetes.** Studies indicate that Medicare costs for people with diabetes are double the costs for those without diabetes. In the Medicaid population and among the uninsured, the cost ratios are four to one. In most other groups, costs are triple those of people without the disease.

Pre-diabetes

Pre-diabetes is diagnosed when blood glucose levels are higher than normal but not yet high enough to be diagnosed as diabetes [Impaired Fasting Glucose (IFG) of 100-125 mg/dL or Impaired Glucose Tolerance (IGT) 2-h plasma glucose 140-199 mg/dL)]. The American Diabetes Association estimates that 79 million people in the U.S. have this condition that puts them at increased risk for diabetes and cardiovascular complications. Patients with pre-diabetes should be screened annually with fasting plasma glucose or A1C.

Diabetes Screening Protocol

The diagnosis of diabetes is based on the measurement of glucose values or, more recently, hemoglobin A1c (A1C) levels. The intent of establishing diagnostic thresholds was to identify people at risk for the complications of diabetes, both micro- and macrovascular, and to introduce effective measures to lower this risk. Many studies have shown that the cumulative risk for diabetes complications is a continuum, but the risk of microvascular complications begins to increase when fasting glucose values equal or exceed 126 mg/dL or A1C $\geq$6.5%.

It is vitally important to recognize that a premature diagnosis of diabetes can have devastating economic and insurance (both health and life) consequences for the patient. The inherent variability of point-of-care testing for blood glucose and A1C precludes its use for the diagnosis of diabetes. Additionally, there are a variety of methods used to measure A1C levels, but only the results from laboratories that use the methodology and standards employed in the Diabetes Control and Complications Trial can be diagnostic. The laboratory report should reflect the methodology used.

Lastly, biologic variability plays a role in the diagnosis of diabetes. All diagnostic tests (fasting glucose, oral glucose tolerance test, A1C, and random plasma glucose) must be repeated and found to be abnormal before a diagnosis can be made unless there are clear symptoms of diabetes (polyuria, polydipsia) and the random glucose is greater than 200 mg/dL.

Random glucose levels in asymptomatic patients are problematic because the condition under which the blood sample was obtained (meal composition and timing) is not standardized. In order to formally diagnose a patient with an abnormality in glucose tolerance or diabetes, either repeated fasting glucose values, A1C, or a 75-gram oral glucose tolerance test should be performed.

The diagnosis of pre-diabetes should alert the provider to counsel the patient about lifestyle modifications and the patient to heed the advice. Pre-diabetes is also associated with a significant risk of progression to overt diabetes, and patients with pre-diabetes should be screened for diabetes at least annually with the screening method that is most cost-effective and clinically relevant to the setting in which a patient is seen.

NOTE: When ordering follow-up testing for one abnormal plasma glucose, use ICD-9 code 790.29 (hyperglycemia) or 790.6 (abnormal chemistry). DO NOT use 250.XX or the patient could be labeled as having diabetes regardless of the test result.

Correlation of A1C with Estimated Average Glucose Levels[1]		
A1C (%)	Estimated Average Glucose (mg/dL)†	95% Confidence Intervals (mg/dL)
5	97	76-120
6	126	100-152
7	154	123-185
8	183	147-217
9	212	170-249
10	240	193-282
11	169	217-314
12	298	240-347

1. Nathan DM et al. *Diabetes Care* 2008;31:1473-1478.
†Estimated Average Glucose = 28.7 x A1C − 46.7

Diagnostic Criteria for Diabetes in Non-Pregnant Adults				
Parameter	Normal	Abnormality of Glucose Metabolism	Diabetes	Comments
Fasting glucose (mg/dL)	<100	100-125	≥126	Testing must be repeated on a separate day.
OGTT 2hr value (mg/dL)	<140	140-199	≥200	75-gram oral glucose tolerance test
Random glucose (mg/dL)	<140		≥200	Patient must have symptoms of hyperglycemia (polyuria, polydipsia, etc). Repetition not needed.
Hemoglobin A1c (%)	<5.7	5.7-6.4	≥6.5	Hemoglobin A1c must be measured according to DCCT standards.

Risk Factors and Screening
Testing should be considered in all adults who are overweight (BMI > 25 kg/m^{2}*) and have one or more additional risk factors:
• Physical inactivity • First-degree relative with diabetes (parent or sibling) • Members of a high-risk ethnic population (African Americans, Hispanic/Latino, Native Americans, Asian Americans, and Pacific Islanders) • Women who have delivered a baby weighing ≥9 lbs or were diagnosed with gestational diabetes (GDM) • Previously identified impaired glucose tolerance (IGT), impaired fasting glucose (IFG), or have had an A1C ≥5.7% according to DCCT standards. • Hypertension (≥140/90 mmHg) or are on therapy for hypertension • HDL cholesterol <35 mg/dl and/or a triglyceride level >250 mg/dL • Women with polycystic ovary syndrome (PCOS) • Other clinical conditions associated with insulin resistance (e.g., severe obesity and acanthosis nigricans) • History of cardiovascular disease (CVD)
In the absence of above risk factors, begin testing for diabetes at age 45 and retest every 3 years. *At-risk BMI may be lower in some ethnic groups

The Role of A1C in Diabetes Management

The formation of hemoglobin A1c (A1C) is non-enzymatic and represents a mass-action reaction that depends on the life span of red blood cells and ambient blood glucose levels. A1C is considered an indicator of the overall trend of glucose values for the previous three months. Monitoring of glycemic status is considered a cornerstone of diabetes care and affects how physicians and patients adjust medical therapy as well as behavioral therapy (e.g., diet and exercise). The better the diabetes control, the lower the A1C, and the fewer the complications. The level of A1C can also be used to call into question the patient's home monitoring of glucose values if a handwritten log is brought to clinic for review. Keep in mind that conditions that reduce red blood cell survival (e.g., hemolytic anemia, hemoglobinopathy, pregnancy, use of certain medications), recent blood transfusions, or the use of erythropoietin analogs will significantly reduce A1C levels.

In 2012, the ADA completely revised its recommendations by proposing a patient-centered tactic for type 2 diabetes therapy. The ADA is now advocating individualized treatment plans similar to those promulgated in the current Utah Diabetes Practice Recommendations. Specifically, the ADA advised an approach that starts with metformin followed by a second or even third oral or injectable agent, with the goal of reducing side-effects or hypoglycemia. The ADA also emphasized the role of insulin, whether in combination with oral agents or alone in management. Most importantly, the group advocated a flexible A1C target based on the patient's attitude, risks of hypoglycemia, potential side-effects, disease duration, presence of micro- or macrovascular complications, resources, and support systems.

GOAL: *A1C below 7%* or as low as possible without significant hypoglycemia.*

A1C <7%* **(Good control)**

- No changes in management indicated (if no excessive hypoglycemia)
- Reinforce previous education

Follow-up A1C:
- If on oral or no medications: at least every 6-12 months
- If on insulin: every 3-6 months

A1C ≥7%* **(Inadequate control)**

- Initiate or adjust medications
- Consult diabetes educator & dietitian

Follow-up A1C: Every 3 months

If A1C >8% for 6-9 months, consider consultation with endocrinologist or diabetologist

*A higher goal may be necessary for certain individuals from special populations.

(American Association of Clinical Endocrinologists and European Association for the Study of Diabetes suggest <6.5%. For A1C >7%, see Inzucchi S, Bergenstal RM, Buse JB et al. 2012. Management of hyperglycemia in type 2 diabetes: a patient-centered approach. *Diabetes Care 35*:1364-1379.)

Overview of Medical Management

Confirmed Diabetes

1. Educate on lifestyle: Refer to diabetes educator/dietitian
2. Initiate self-monitoring blood glucose (SMBG)
3. Check A1C
4. Screen for complications

Note: Optimal control means A1C <7.0%*; FPG 70-130 mg/dL. *See page 8 for discussion of patient-centered treatment.

If FPG is normal but A1C is high, consider postprandial glucose (PPG) monitoring.

Ketosis or volume depletion	FPG >300mg/dL without ketosis	FPG ≤300mg/dL and relatively asymptomatic
Consider hospital admission	Strongly advise insulin therapy (pg 10-14)	Metformin, lifestyle, diabetes education, A1C

Follow Up
Visit A1C > 7%*

Individually Assess Patient Characteristics*
- patient goals • weight effects • cost • age
- relative efficacy • cardiac, renal, and hepatic functions

*Bariatric surgery should be considered if BMI >35 kg/m² if diabetes or associated co-morbidities are difficult to control with lifestyle and pharmacologic therapy [ADA *Diabetes Care.* 2012 Jan;35 (suppl 1)].

Continue metformin

Possible weight increase, greater A1C lowering (>1%), principally reduce fasting glucose

Possible weight loss or neutral, less A1C lowering (<1%), principally reduce postprandial glucose

Basal insulin
(Most effective)

OR

Sulfonylureas (SU)
(Least expensive)

OR

Thiazolidinediones (TZDs)
(No hypoglycemia)
Note: TZDs as a class increase the risk of fractures, heart failure, and macular edema

Not Included:
- Alpha-glucosidase inhibitors
- Pramlintide
- Glinides

DPP-IV inhibitor
(Least effective)

OR

GLP-1 analogs
(Most weight loss)

Medication Class	Expected A1C Lowering (%)[1,2]	Comments
Biguanides (metformin)	1.5	Contraindicated in renal, cardiac, and respiratory failure. Unless contraindications or side effects develop, metformin should be continued through pharmacological escalation
Sulfonylureas	1.5	Hypoglycemia, weight gain
Thiazolidinediones (pioglitazone)	0.8-1.0	Weight gain, edema, CHF (especially with insulin); there may be an increase in myocardial infarction with use of Rosiglitazone.
Dipeptidyl peptidase-4 (DPP-IV) Inhibitors	0.5-0.9	Initially reduce sulfonylurea dose by 50%; do **not** use with GLP-1 analogs
Glucagon-like peptide (GLP-1) Analogs	0.6	Generally associated with weight loss; recently FDA approved for use with a basal insulin
Insulin	≥2.5	Most effective; possible hypoglycemia, weight gain

Insulin Therapy

The following pages provide a brief overview of the advantages and disadvantages of various insulin therapies as well as guidance on initiating treatment. Insulin profiles below show current formulas available. Mixed short- and long-acting insulins are also available for pre-mixed regimens.

> **Patients with type 1 DM should be started on insulin therapy upon diagnosis. These patients respond best to physiologic therapy (pg 13).**

Comparative Profiles of Insulin

Type	Generic (Brand) Name	Onset	Peak	Usual Effective Duration	AWP Cost*
Rapid Acting	Aspart (Novolog)	10-20 min	1-2 hrs	Up to 5 hrs	10 ml: $129 FlexPen®/Penfill 3 ml (in packages of 5): $249
	Glulisine (Apidra)	10-20 min	1-2 hrs	Up to 5 hrs	10 ml: $112 SoloSTAR® pen 3 ml (in packages of 5): $216
	Lispro (Humalog)	10-20 min	1-2 hrs	Up to 5 hrs	10 ml: $129 KwikPen® 3 ml (in packages of 5): $249
Regular (short acting)	Novolin R Humulin R	30-60 min	2-3 hrs	4-8 hrs	10 ml: $65 10 ml: $65
Intermediate Acting	NPH (Novolin N) NPH (Humulin N)	2-4 hrs	4-10 hrs	10-16 hrs	10 ml: $65 10 ml: $65
Pre-mix	70/30 (NovoLog Mix) 75/25 (Humalog Mix) 50/50 (Humalog Mix) 70/30 Humulin 70/30 Novolin 70/30 NPH/Regular	5-15 min	Varies	10-16 hrs	Varies
Peakless	Detemir (Levemir)	~2 hrs	8-10 hrs	16-20 hrs	10 ml: $121 FlexPen® 3 ml (in packages of 5): $233
	Glargine (Lantus)	1 hr	Relatively peakless	18-24 hrs	10 ml: $119 SoloSTAR® pen 3 ml (in packages of 5): $230
	1000 units = 1 vial = 10 mL				*per January 2011 AWP or MAC, where available

Basal Insulin Therapy for Type 2 Diabetes

Consider if treatment naive and A1C >10 or FPG >260 or oral agent failure with A1C >8.5

Patients with type 2 diabetes whose blood glucose is not well controlled with oral agents, diet, and exercise should begin insulin therapy. Confusion over appropriate starting doses may lead to clinical inertia. Insulin therapy must be individualized to the patient; titration may be a lengthy process. Although the dose of oral medications may be reduced or even discontinued once insulin is started in patients with type 2 DM, combination therapy with metformin (plus or minus SUs) should be continued to:

- Improve glucose control,
- Minimize weight gain, and
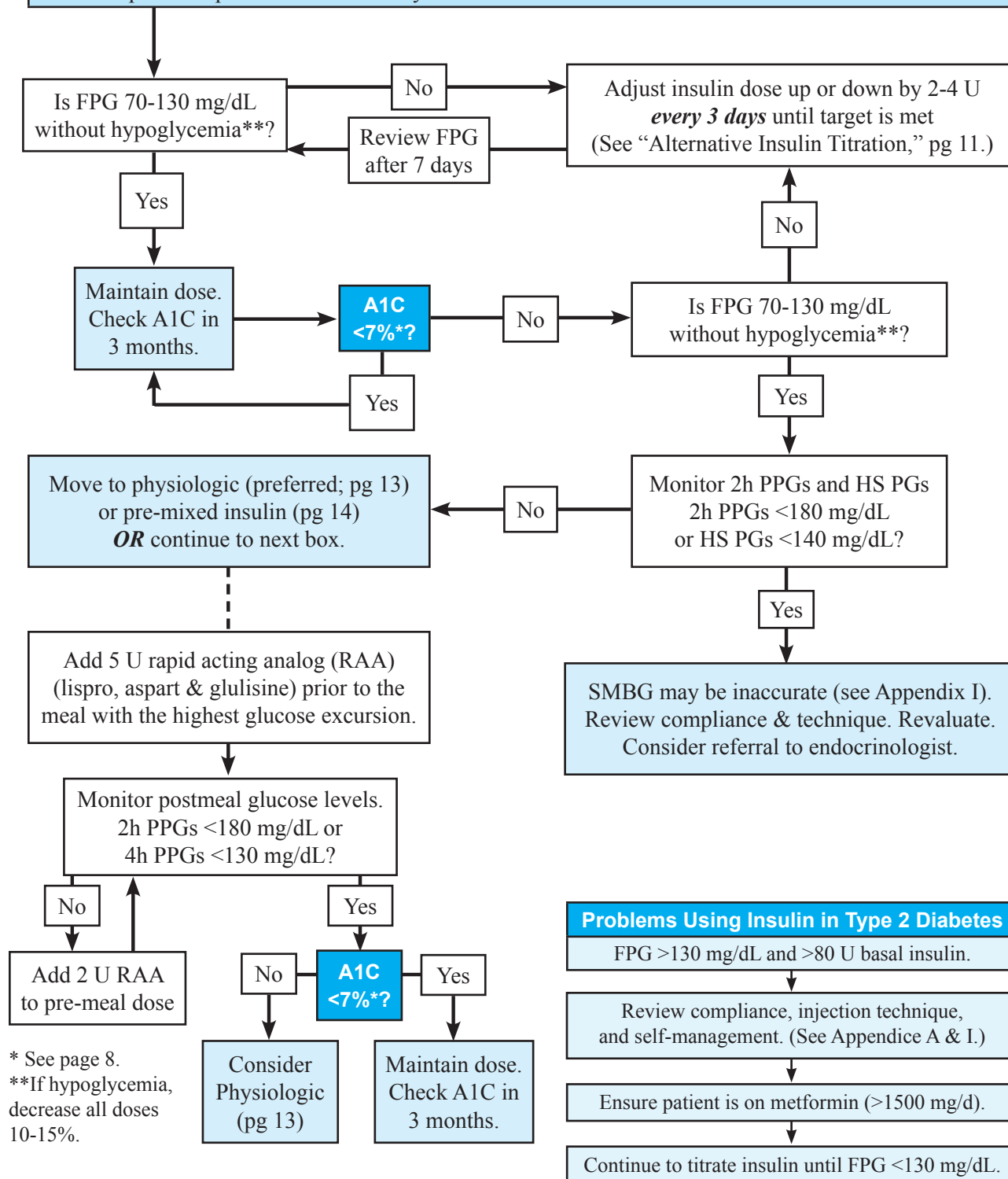- Decrease insulin need.

Principles

- Glargine, NPH (HS administration), or detemir (HS administration) should be used to control fasting plasma glucose (FPG). See page 10 "Comparative Profiles of Insulin."

- Sulfonylureas could be continued to control daytime PPGs.

- Once FPG is controlled with insulin, the daytime PG (plasma glucose) readings will frequently come under control with oral agents. If daytime PGs do NOT come under control, move to physiologic insulin therapy (page 13).

- Be cautious using thiazolidinediones (TZDs) with insulin due to fluid accumulation and possibility of heart failure.

- Patients may still experience poor glucose control while on large doses of basal insulin (>80 U). If FPG remains significantly greater than 130 mg/dL, the patient may benefit from referral to a diabetes educator for self-management education (Appendix A). Review compliance and injection technique with patient. Certain patients may benefit from >1500 mg metformin daily. Continue to titrate basal insulin until FPG <130 mg/dL.

Alternative Insulin Titration	
Start with 10-15 U/day and adjust weekly	
Mean of FPG values from preceding 2 days	Increase insulin dose/day
>180 mg/dL	8 units
140-180 mg/dL	6 units
120-139 mg/dL	4 units
100-119 mg/dL	2 units
Riddle MC et al: *Diabetes Care* (2003) 26: 3080-86	

Using Insulin in Type 2 Diabetes

Patient Requires Basal Insulin Therapy

- Optimize oral doses (metformin may be optimized up to 2000 mg/day in certain patients)
- Insulin starting dose: 10-15 U or 0.2 U/kg of detemir (HS), glargine (AM, PM, *or* HS), *or* NPH (HS)
- Teach injection technique and *self-management for hypoglycemia* (refer to diabetes educator for insulin start)
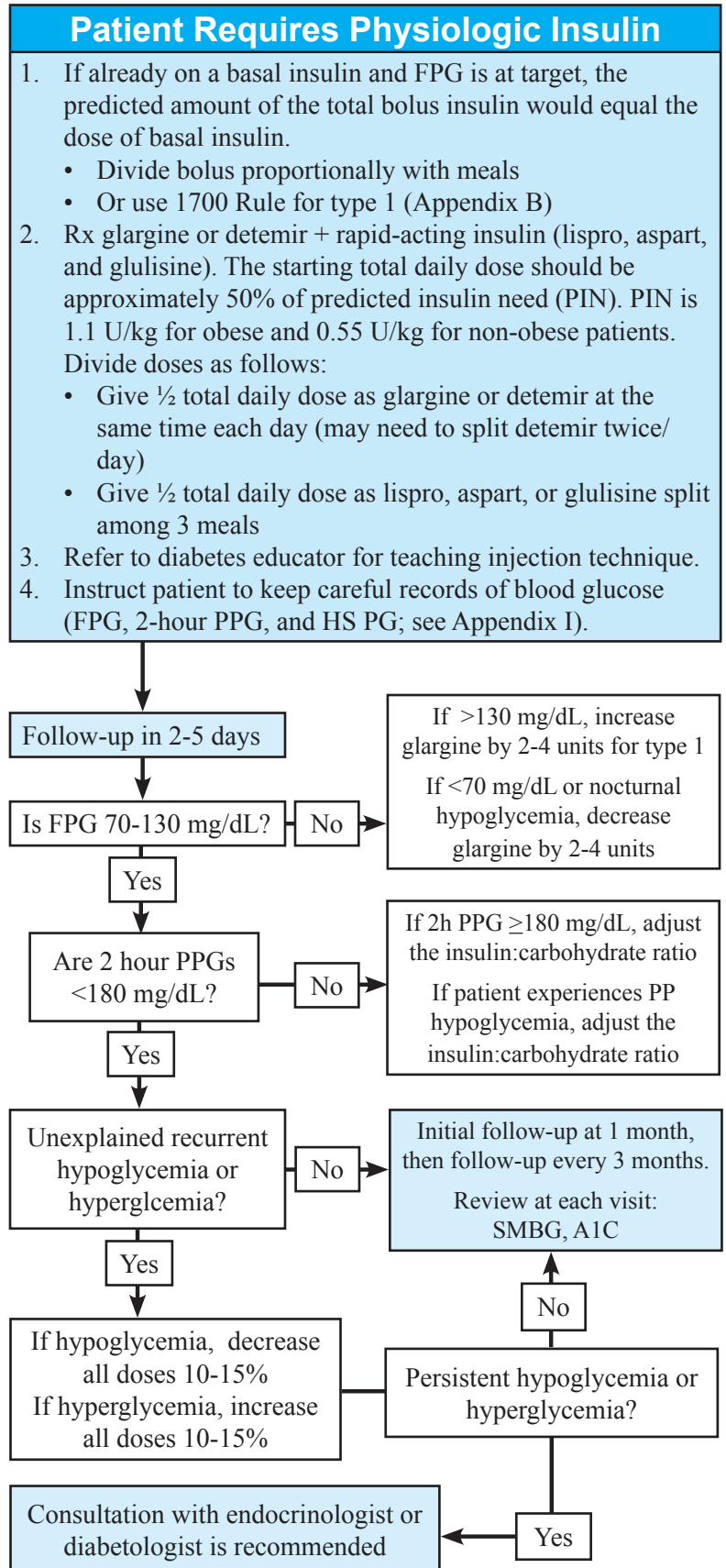- Have patient report FPG after 2-3 days

Is FPG 70-130 mg/dL without hypoglycemia**? — **No** → Adjust insulin dose up or down by 2-4 U *every 3 days* until target is met (See "Alternative Insulin Titration," pg 11.)

Review FPG after 7 days

Yes ↓

Maintain dose. Check A1C in 3 months.

A1C <7%*? — **No** → Is FPG 70-130 mg/dL without hypoglycemia**?

No (from Adjust insulin dose box)

Yes (A1C) → back to Maintain dose.

Is FPG 70-130 mg/dL without hypoglycemia**? — **Yes** ↓

Monitor 2h PPGs and HS PGs 2h PPGs <180 mg/dL or HS PGs <140 mg/dL?

No → Move to physiologic (preferred; pg 13) or pre-mixed insulin (pg 14) *OR* continue to next box.

Yes ↓

SMBG may be inaccurate (see Appendix I). Review compliance & technique. Revaluate. Consider referral to endocrinologist.

Add 5 U rapid acting analog (RAA) (lispro, aspart & glulisine) prior to the meal with the highest glucose excursion.

↓

Monitor postmeal glucose levels. 2h PPGs <180 mg/dL or 4h PPGs <130 mg/dL?

No → Add 2 U RAA to pre-meal dose

Yes ↓

A1C <7%*? — **No** → Consider Physiologic (pg 13)

Yes → Maintain dose. Check A1C in 3 months.

* See page 8.
**If hypoglycemia, decrease all doses 10-15%.

Problems Using Insulin in Type 2 Diabetes

FPG >130 mg/dL and >80 U basal insulin.

↓

Review compliance, injection technique, and self-management. (See Appendice A & I.)

↓

Ensure patient is on metformin (>1500 mg/d).

↓

Continue to titrate insulin until FPG <130 mg/dL.

Physiologic (Basal/Bolus) Insulin Therapy
for Type 1 or Type 2 Diabetes

Principles

- This more intensive insulin regimen provides the closest approximation to normal insulin physiology. It uses glargine or detemir insulin for basal metabolic control, and lispro, aspart, or glulisine for prandial control and correction of high glucose levels.

  - Glargine or detemir is used to control glycemia in the basal state when not eating; e.g., the period from bedtime until breakfast. Bedtime snacking is NOT recommended.
  - Rapid-acting insulin (lispro, aspart, or glulisine) is added at mealtime. (See algorithm page 12.) This insulin is adjusted to prevent postprandial hyperglycemia or hypoglycemia. Plasma glucose 4 hours after a meal should be <130 mg/dL. Adjust testing and advise on correction based on information.
  - Discontinue sulfonylureas when adding prandial insulin.
  - Pre-meal rapid-acting doses are usually determined by carbohydrate counting and use of a carbohydrate ratio. An equally effective strategy in type 2 diabetes is pre-meal insulin based on a fixed meal plan. In either case, training in medical nutrition therapy by a qualified dietitian and training in insulin use by a qualified diabetes educator are recommended for success.

- Nearly all type 1 patients should be on physiologic (basal plus bolus) regimens. Most type 2 patients requiring insulin will also benefit from physiologic insulin.

- Instruction for modifying insulin doses for exercise and sick days should be incorporated into the regimen.

Patient Requires Physiologic Insulin

1. If already on a basal insulin and FPG is at target, the predicted amount of the total bolus insulin would equal the dose of basal insulin.
   - Divide bolus proportionally with meals
   - Or use 1700 Rule for type 1 (Appendix B)
2. Rx glargine or detemir + rapid-acting insulin (lispro, aspart, and glulisine). The starting total daily dose should be approximately 50% of predicted insulin need (PIN). PIN is 1.1 U/kg for obese and 0.55 U/kg for non-obese patients. Divide doses as follows:
   - Give ½ total daily dose as glargine or detemir at the same time each day (may need to split detemir twice/day)
   - Give ½ total daily dose as lispro, aspart, or glulisine split among 3 meals
3. Refer to diabetes educator for teaching injection technique.
4. Instruct patient to keep careful records of blood glucose (FPG, 2-hour PPG, and HS PG; see Appendix I).

Follow-up in 2-5 days

Is FPG 70-130 mg/dL? — No →
If >130 mg/dL, increase glargine by 2-4 units for type 1
If <70 mg/dL or nocturnal hypoglycemia, decrease glargine by 2-4 units

Yes ↓

Are 2 hour PPGs <180 mg/dL? — No →
If 2h PPG ≥180 mg/dL, adjust the insulin:carbohydrate ratio
If patient experiences PP hypoglycemia, adjust the insulin:carbohydrate ratio

Yes ↓

Unexplained recurrent hypoglycemia or hyperglcemia? — No →
Initial follow-up at 1 month, then follow-up every 3 months.
Review at each visit: SMBG, A1C

Yes ↓

If hypoglycemia, decrease all doses 10-15%
If hyperglycemia, increase all doses 10-15%

Persistent hypoglycemia or hyperglycemia? — No ↑

Yes →

Consultation with endocrinologist or diabetologist is recommended

Pre-mixed Therapy for Type 2 Diabetes

Principles

- These insulin regimens are *NOT* designed to mimic normal insulin physiology and are *NOT* recommended for type 1 patients.

- These insulin regimens are sometimes adequate for control of type 2 patients for whom maximum efforts with oral medications or oral medications plus basal insulin are not effective.

- These insulin regimens are sometimes chosen when patients are not able to involve themselves in a physiologic multiple daily dose regimen.

- **Consistency with meals** (same time daily, carb content, and caloric content) and adequate adherence to a medical nutrition therapy plan are important to success and safety of all insulin regimens, and especially with pre-mixed insulin.

- Patients on these insulin therapy regimens should move to physiologic (basal/bolus) insulin if goals are not met with these types of insulin therapy regimens.

- These regimens are less convenient for patients and may not offer the best glucose control (more prone to hyperglycemia); however, the lower cost associated with pre-mixed insulin therapy may increase compliance among patients unable to afford more expensive therapies.

Pre-mixed Insulins Available

All of the following are BID (pre-breakfast and pre-supper). Short-acting insulins should *NOT* be administered at bedtime.

- Humulin 70/30 or Novolin 70/30

- 70/30 (NPH/Regular)

- Novolog (aspart) Mix 70/30

- Humalog (lispro) Mix 75/25

- Humalog (lispro) Mix 50/50

See also page 10, "Comparative Profiles of Insulin."

Additional Resources

- Insulin Algorithm for Type 2 Diabetes Mellitus in Children and Adults/Initiation of Once Daily Insulin Therapy for Type 2 DM http://www.tdctoolkit.org/tdc_publications/algorithms_and_guidelines/insulin_algorithm_for_type_2_diabetes_mellitus_in_children_and_adults.asp

- Texas Diabetes Council illustrates a variety of start scenarios with case studies. http://www.dshs.state.tx.us/diabetes/PDF/algorithms/INST2.pdf

- Algorithm from *Diabetes Spectrum* 2009;22:85-91 (page90) http://care.diabetesjournals.org/content/32/1/193.full.pdf+html

Overview of Cardiovascular Disease in Diabetes

Patients with diabetes have a 2- to 4-fold increased risk of cardiovascular disease (CVD). The increased risk for CVD is much more dramatic in women with diabetes. All individuals with diabetes have a higher fatality rate once they have CVD.

Research has established that modification of certain risk factors commonly associated with diabetes can substantially reduce the risk of cardiovascular disease. Well-established interventions are listed below. Persons with diabetes benefit from these interventions to an extent that exceeds that seen in patients without diabetes.

- Lifestyle modification (tobacco cessation, increased physical activity, Medical Nutritional Therapy including weight loss, if appropriate)
- Control of blood pressure
- LDL cholesterol lowering
- Anti-platelet therapy
- Glycemic control (limited effect on risk reduction)

Table: Interventions to Reduce Cardiovascular Risk in Diabetes	
	Relative Risk Reduction
Statins	$\geq 20\%$
Antihypertensive therapy	$\geq 20\%$
Glycemic control	10-15%
Aspirin:	
2° prevention	20%
1° prevention	Approximately 10%
Smoking cessation	7-47%
ACE inhibitors/ARBs	Unknown
Beta blockers:	
Post-MI, 1st 2y	30%
Stable CHD	Unknown

Multifactorial Interventions to Reduce Cardiovascular Risk

Analyses of the UKPDS and Steno-2 trials indicate that statins and blood pressure-lowering drugs reduce cardiovascular events to a greater extent than anti-hyperglycemic treatments that reduce A1C levels to about 7%. More intensive glycemic control to A1C levels of 6.0-6.5% in persons with established type 2 diabetes may modestly lower CVD events by an additional 9%, but at the expense of a more than two-fold greater risk of severe hypoglycemia. Comprehensive interventions to reduce LDL-cholesterol, systolic blood pressure, and A1C can reduce total and cardiovascular mortality by about 50% over 10-15 years.

Aspirin and Diabetes Care

For secondary prevention in persons with atherosclerotic vascular disease with or without concurrent diabetes, low-dose aspirin provides a substantial 20% relative risk reduction (RRR) and 1.5% per year absolute risk reduction (ARR) in recurrent cardiovascular disease (CVD) events, including myocardial infarction and stroke. However, for primary prevention the relative and absolute benefits of aspirin are much lower with just a 12% RRR and 0.06% per year ARR in CVD events. For primary prevention in persons with diabetes, recent randomized trials and meta-analyses of available trials have found a similar—but not statistically significant—10% RRR in CVD events. Given the uncertain efficacy of aspirin for primary prevention of CVD in adults with diabetes and its recognized risk for upper gastrointestinal bleeds and hemorrhagic stroke, a 2010 expert consensus document from the American Diabetes Association, American Heart Association, and American College of Cardiology suggested that aspirin utilization for primary prevention be guided by a combined assessment of either age, sex, and other CVD risk factors or by an estimate of absolute 10-year CVD risk. (See Table: Aspirin Recommendations, next page.)

Table: Aspirin Recommendations for Patients with No History of CVD or at Increased Risk of Bleeding (No history of prior gastrointestinal bleeding, no prior peptic ulcer disease, or no concurrent warfarin/NSAID therapy)			
Recommendation Based on Calculated 10-year CVD Risk*			
Aspirin should be **avoided**			< 5% risk
Aspirin may be **considered**			5-10% risk
Aspirin is **reasonable**			> 10% risk

* Risk may be calculated at http://zunis.org/FHS_CVD_Risk_Calc_2008.htm or http://www.dtu.ox.ac.uk/riskengine/index.php

Note: There is concern that these risk calculators may overestimate CVD risk in modern populations with diabetes that receive more intensive treatment of lipids and hypertension than in the 1990s.

Recommendation Based on Patient Characteristics			
	Gender	Age	Risk factors**
Aspirin should be **avoided**	Male	≤ 50 years	none
	Female	≤ 60 years	none
Aspirin may be **considered**	Male	≤ 50 years	1
		> 50 years	none
	Female	≤ 60 years	1
		> 60 years	none
Aspirin is **reasonable**	Male	> 50 years	≥ 1
	Female	> 60 years	≥ 1

**Risk factors: smoking, hypertension, albuminuria, dyslipidemia, family history

ASPIRIN DOSAGE RECOMMENDATION 75-162 mg/day

ACE/ARB

ACE inhibitors or angiotensin II receptor blockers (ARBs) are first-line therapeutic agents for persons with diabetes who have hypertension, albuminuria, or systolic heart failure. The efficacy of these drugs to reduce cardiovascular events has not been demonstrated in other subgroups of persons with diabetes (with or without CVD) whose other cardiovascular risk factors are controlled.

Beta Blockers

Beta blockers are indicated during the first two years post-myocardial infarction and indefinitely in persons with systolic heart failure. Specific cardioprotection with these agents in persons with stable coronary heart disease with or without concomitant hypertension has not been demonstrated. Newer generation vasodilating beta blockers with neutral effects on insulin resistance (carvedilol, nebivolol) may be preferred.

Cardiovascular Screening

Symptoms of coronary heart disease (CHD) are more likely to be atypical in persons with diabetes, and may include non-exertional chest pain, back pain, arm pain, abdominal pain, shortness of breath, fatigue, or feeling ill without focal symptoms.

Careful evaluation for these atypical symptoms in addition to cardiovascular risk factors may prompt further testing.

Patients with symptoms suggesting CHD should undergo evaluation using appropriate methods. Note: Stress echocardiography is a highly cost-effective screening method for many patients.

The value of screening the truly asymptomatic patient with diabetes for CHD is uncertain. While CHD is much more prevalent among those with diabetes, there is little evidence that screening procedures in asymptomatic persons have a positive effect on outcomes. Intensive medical therapy can provide equal benefit to invasive revascularization in some studies. In addition, silent ischemia may reverse over time with intense medical therapy. A randomized observational study could not demonstrate any clinical benefit from screening asymptomatic patients with type 2 diabetes and a normal ECG.

Cardiovascular screening could be considered in asymptomatic patients with poor exercise capacity, multiple risk factors, or abnormal ECG, especially if the results would alter a current treatment regimen. A mildly abnormal stress test may lead to more aggressive treatment of cardiac risk factors and lifestyle modification, without necessarily requiring invasive evaluation. A severely abnormal stress test should generally be referred for invasive evaluation, even in the absence of clear symptoms. Patients with silent ischemia and multi-vessel CAD or LV dysfunction are at particularly high risk of cardiovascular events, and are at higher risk than similar patients with symptomatic angina.

> **All persons with diabetes should have cardiovascular risk factors assessed at least annually and treated accordingly.**

Additional Resources

For the latest evidenced-based clinical practice guidelines for hypertension and cholesterol, visit http://www.nhlbi.nih.gov/guidelines/index.htm.

For patient education, American Heart Association offers an interactive program at http://mylifecheck.heart.org/.

References

Stratton IM, Cull CA, Adler AI, et al. Additive effects of glycemia and blood pressure exposure on risk of complications in type 2 diabetes: a prospective observational study (UKPDS 75). *Diabetologia* 2006; 49(8): 1761-1769.

Gaede P, Lund-Andersen H, Parving HH, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. *N Engl J Med* 2008; 358:(6): 580-591.

Nathan DM. The role of glycemia management in the prevention of cardiovascular disease – starting over? *Ann Intern Med* 2009; 151:(12):888-889.

Turnbull FM, Abraina C, Anderson RJ, et al. Intensive glucose control and macrovascular outcomes in type 2 diabetes. *Diabetologia* 2009; 52(11): 2288-2298.

American Diabetes Association. Standards of medical care in diabetes–2012. *Diabetes Care* 2012;35(Suppl 1).

Pignone M, Alberts MJ, Colwell JA, et al. Aspirin for primary prevention of cardiovascular events in people with diabetes: A position statement of the American Diabetes Association, a scientific statement of the American Heart Association, and an expert consensus document of the American College of Cardiology Foundation. *Circulation* 2010; 121:2694-2701.

Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomized trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009; 338:b1665.

Young, LH, et al. Outcomes After Screening for Asymptomatic Coronary Artery Disease in Patients With Type 2 Diabetes *JAMA*. 2009;301(15):1547-1555.

Diabetes and Hypertension

Prevalence and Control

The overall prevalence of hypertension in diabetes patients stabilized over the past decade, but hypertension control rates did *not* improve over this period and remain disappointingly low. Comparing data from 2001 to 2008, the National Health and Nutrition Examination Survey (NHANES) found that the prevalence of hypertension in diabetes— defined in this study as ≥140/90 mmHg rather than ≥130/80 mmHg—remained stable at about 68% (79% in blacks and 61% in Hispanics). The exception was a dramatic increase in hypertension prevalence from 27% to 43% in persons with diabetes aged 20-44 years, possibly driven by the obesity epidemic. Just 54% of persons with diabetes and hypertension (52% of blacks and 45% of Hispanics) have their BP controlled to <140/90 mmHg, let alone to <130/80 mmHg.[9] These continued poor hypertension control rates, which are worse in racial and ethnic minorities, are of particular importance since new data demonstrate that excess cardiovascular risk in diabetes is driven primarily by hypertension rather than by hyperglycemia or dyslipidemia.[10] Aggressive management should allow at least 70% of persons with diabetes and hypertension to have their BP controlled below 130/80 mmHg.[11]

BP Goals for Persons with Diabetes		
	Office, mmHg	Home, mmHg
Most patients with diabetes	<130/80	<130/80
Selected patients (see Annotation 3 below)	<140/90	<135/85

Unfortunately, only 50% of hypertensive men and just 42% of hypertensive women who have diabetes currently have their BP controlled to <130/80 mmHg; however, control rates of nearly 70% have been achieved in clinical trials (eg., the ACCOMPLISH and GEMINI trials) utilizing aggressive management strategies.

Diagnosis

Because of the frequent occurrence of white-coat hypertension (elevated office BP but normal out-of-office BP) and the reverse phenomenon, masked hypertension (high normal office BP but elevated out-of-office BP), out-of-office BP measurement with either 24-hour ambulatory BP monitoring (ABPM) and/or standardized home BP monitoring (HBPM) is a stronger predictor than office BP of future adverse cardiovascular and renal events.[12,13] White coat hypertension has a prognosis similar to that of normotension, while masked hypertension has an adverse prognosis nearly equivalent to sustained hypertension.[12,13] Current national and international guidelines therefore favor the use of out-of-office BP monitoring to detect these phenomena and accurately confirm the diagnosis of hypertension in many patients.[14-17] In contrast, the 2012 ADA guideline continues to recommend that the diagnosis of hypertension be made on the basis of carefully measured BP ≥130/80 mmHg on two office visits.[18] The ADA discourages the use of ABPM and HBPM, citing the relatively limited data using these modalities to diagnose hypertension in persons with diabetes. See algorithm, page 20.

Therapeutic Goal

Optimal goal BP in persons with diabetes remains uncertain in 2012. An "individualized" approach continues to be recommended by the most recent clinical guidelines from the American Diabetes Association (2012)[1], American Association of Clinical Endocrinologists (2011)[2], and the Canadian Hypertension Education Program (2011)[3]: (1) Target BP < 130/80 mmHg for most patients (2) Lower or higher target BPs for selected patients, although specific target BPs and selection criteria are not fully detailed in these guidelines.

A target BP < 130/80 mmHg may be particularly considered in subgroups of persons with diabetes and hypertension: (1) a target systolic BP < 120-130 mmHg in patients at high risk of stroke, including patients with a prior stroke or TIA, family history of stroke, known severe (> 70%) carotid stenosis,

or on anticoagulation therapy with an increased risk of intracerebral hemorrhage[4] (2) a target systolic BP < 130/80 mmHg in patients with GFR < 45-60 ml/min/1.73m2 and albuminuria > 300-1000 mg/day.[5] The American College of Cardiology/American Heart Association 2011 guidelines on hypertension in the elderly suggest a target systolic BP of 140-145 mmHg in octogenarians.[6] Finally, a BP < 115/70 should be avoided in patients with type 2 diabetes, hypertension, and coronary heart disease.[7,8]
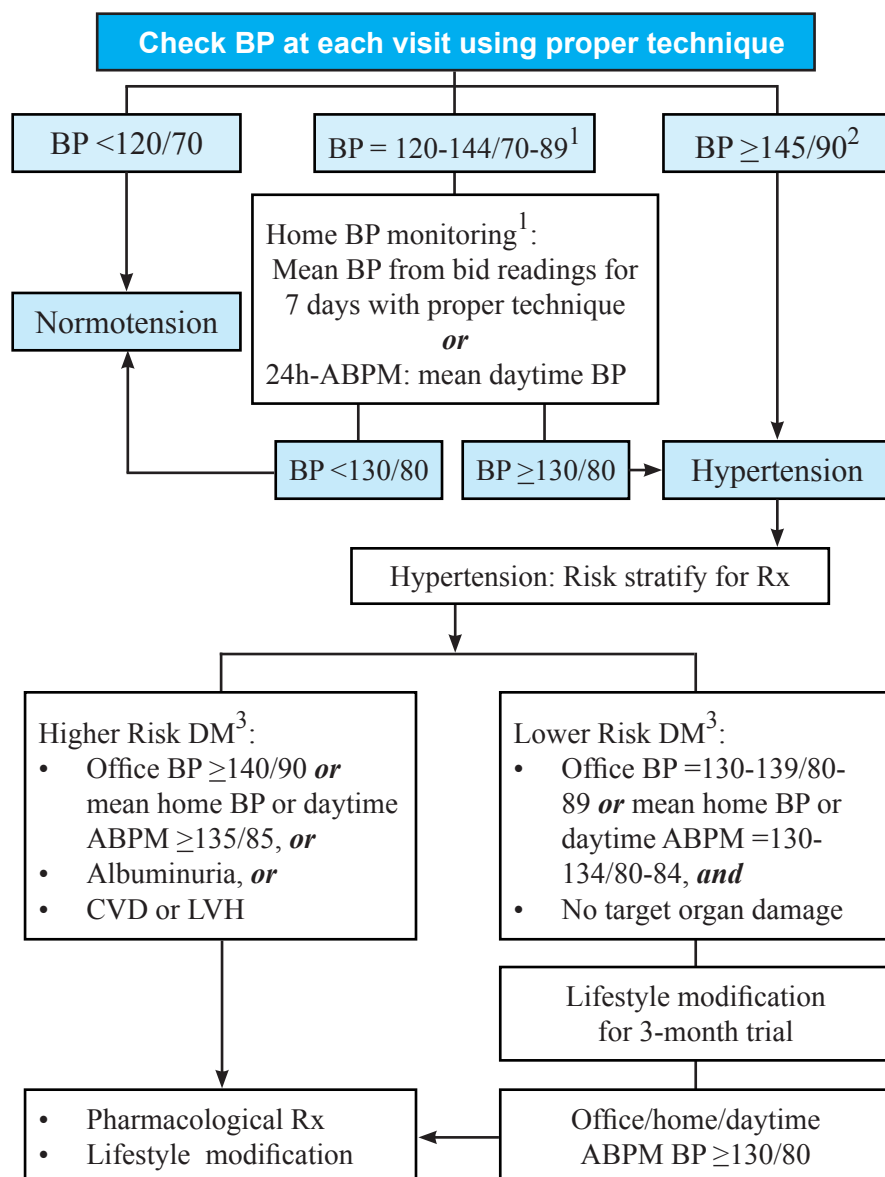
References

1. American Diabetes Association. Standards of medical care in diabetes—2012. *Diabetes Care* 2012; 35(Suppl 1): S11-S63.

2. Handelsman Y, Mechanick JI, Blonde L, et al. AACE Task Force for developing a diabetes comprehensive care plan: AACE Diabetes Care Plan Guidelines. *Endocrine Practice* 2011; 17(Supple 2): 3-53.

3. Canadian Hypertension Education Program. The 2011 Canadian Hypertension Education Program Recommendations for the management of hypertension: blood pressure measurement, diagnosis, assessment of risk, and therapy. *Can J Cardiol* 2011; 27:415-433.

4. Genuth S and Ismail-Beigi F. Clinical implications of the ACCORD Trial. *J Clin Endocrinol Metab* 2012; 97; 41-48.

5. Upadhyay A, Earley A, Haynes SM, et al. Systematic review: blood pressure target in chronic kidney disease and proteinuria as an effect modifier. *Ann Intern Med* 2011; 154:541-548.

6. Aronow WS, Fleg JL, Pepine CJ, et al. The ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *Circulation* 2011; 123:2434-2506.

7. Cooper-Dehoff RM, Gong Y, Handberg EM, et al. Tight blood pressure control and cardiovascular outcomes among hypertensive patients with diabetes and coronary artery disease. *JAMA* 2010; 304:61-68.

8. Redon J, Mancia G, Sleight P, et al. Safety and efficacy of low blood pressures among patients with diabetes: subgroup analyses from the ONTARGET Trial. *J Am Coll Cardiol* 2012; 59:74-83.

9. Wang J, Geiss LS, Cheng YJ, et al. Long-term and recent progress in blood pressure levels among U.S. adults with diagnosed diabetes, 1988-2008. *Diabetes Care* 2011; 34:1579-1581.

10. Chen G, McAlister FA, Walker Rh, et al. Cardiovascular outcomes in Framingham participants with diabetes: the importance of blood pressure. *Hypertension* 2011; 57:891-897.

11. ACCORD Study Group. Effects of intensive blood pressure control in type 2 diabetes mellitus. *N Engl J Med* 2010; 362:1575-1585.

12. O'Brien E. Twenty-four-hour ambulatory blood pressure measurement in clinical practice and research: a critical review of a technique in need of implementation. *J Intern Med* 2011; 269: 478-495.

13. Stergiou GS, Parati G. Home blood pressure monitoring may make office measurements obsolete. *J Hypertens* 2012; 30:463-465.

14. Pickering TG, Miller NH, Ogedegbe G, et al. Call to action on use and reimbursement for home blood pressure monitoring: a joint scientific statement from the American Heart Association, American Society of Hypertension, and Preventive Cardiovascular Nurses Association. *Hypertension* 2008; 52:1-9.

15. Krause T, Lovibond K, Caulfield M, et al. Management of hypertension: summary of NICE guidance. *BMJ* 2011; 343:d4891.

16. Head GA, Mcgrath BP, Mihailidou AS, et al. Ambulatory blood pressure monitoring in Australia: 2011 consensus position statement. *J Hypertens* 2012; 59; 129-135.

17. Canadian Hypertension Education Program. The 2011 Canadian Hypertension Education Program recommendations for the management of hypertension: blood pressure measurement, diagnosis, assessment of risk, and therapy. *Can J Cardiol* 2011; 27:415-433.

18. American Diabetes Association. Standards of medical care in diabetes—2012. *Diabetes Care* 2012; 35(Suppl 1): S11-S63.

A Note on Proper Technique

Most errors in BP measurement technique falsely elevate BP. Use of proper technique may lower BP by 10/5 mmHg:

1. Rest 5 minutes, seated, back supported, feet flat on the floor.
2. No conversation.
3. Use correct cuff size (based on cuff bladder); 50% of adults require a large adult cuff.
4. Place cuff at mid-sternal level with the bladder centered over the brachial artery.
5. Deflate the cuff ≤2-3 mmHg per second.
6. If the first measured BP is ≥130/80 mmHg, repeat it twice at 1 minute intervals; ignore the first reading, which tends to be falsely high, and average the last two readings to better approximate usual BP.
7. Measure standing BP to detect orthostatic hypotension that may limit therapy.

Check BP at each visit using proper technique

BP <120/70 | BP = 120-144/70-89[1] | BP ≥145/90[2]

Home BP monitoring[1]:
Mean BP from bid readings for
7 days with proper technique
or
24h-ABPM: mean daytime BP

Normotension

BP <130/80 | BP ≥130/80 → Hypertension

Hypertension: Risk stratify for Rx

Higher Risk DM[3]:
- Office BP ≥140/90 *or* mean home BP or daytime ABPM ≥135/85, *or*
- Albuminuria, *or*
- CVD or LVH

Lower Risk DM[3]:
- Office BP =130-139/80-89 *or* mean home BP or daytime ABPM =130-134/80-84, *and*
- No target organ damage

Lifestyle modification
for 3-month trial

- Pharmacological Rx
- Lifestyle modification

Office/home/daytime
ABPM BP ≥130/80

Modified From: *Diabetes Care* 2012; 35 (Suppl 1): S11; *Can J Cardiol* 2010; 26:241

Annotations

1. Out-of-office BP monitoring to detect the 30-40% of persons with white-coat or masked hypertension, particularly using the more expensive and less available ABPM approach, is not feasible for all persons with diabetes. A study of 554 subjects with diabetes found that 90% of persons with a *carefully measured* office BP < 120/70 mmHg also had a mean daytime BP < 130/80 mmHg on an ABPM study, confirming normotension.[1] Similarly, 90% of persons with a *carefully measured* office BP ≥ 145/90 mmHg had a mean daytime BP ≥130/80 mmHg on an ABPM study, confirming a diagnosis of hypertension. However, 38% of patients with office BP between 120-144/70-89 mmHg would be *misclassified* as either normotensive or hypertensive if out-of-office BP monitoring were not utilized.[1] This study proposed a new algorithm to more accurately confirm the diagnosis of hypertension in persons with diabetes.[1] In the Figure, their algorithm is modified slightly to incorporate

use of HBPM when ABPM studies are not available. Similarly, the 2011 American Association of Clinical Endocrinologists Diabetes Comprehensive Care Plan suggests consideration of an annual ABPM study to detect white-coat and masked hypertension as well as elevated nocturnal BP in persons with diabetes.[2]
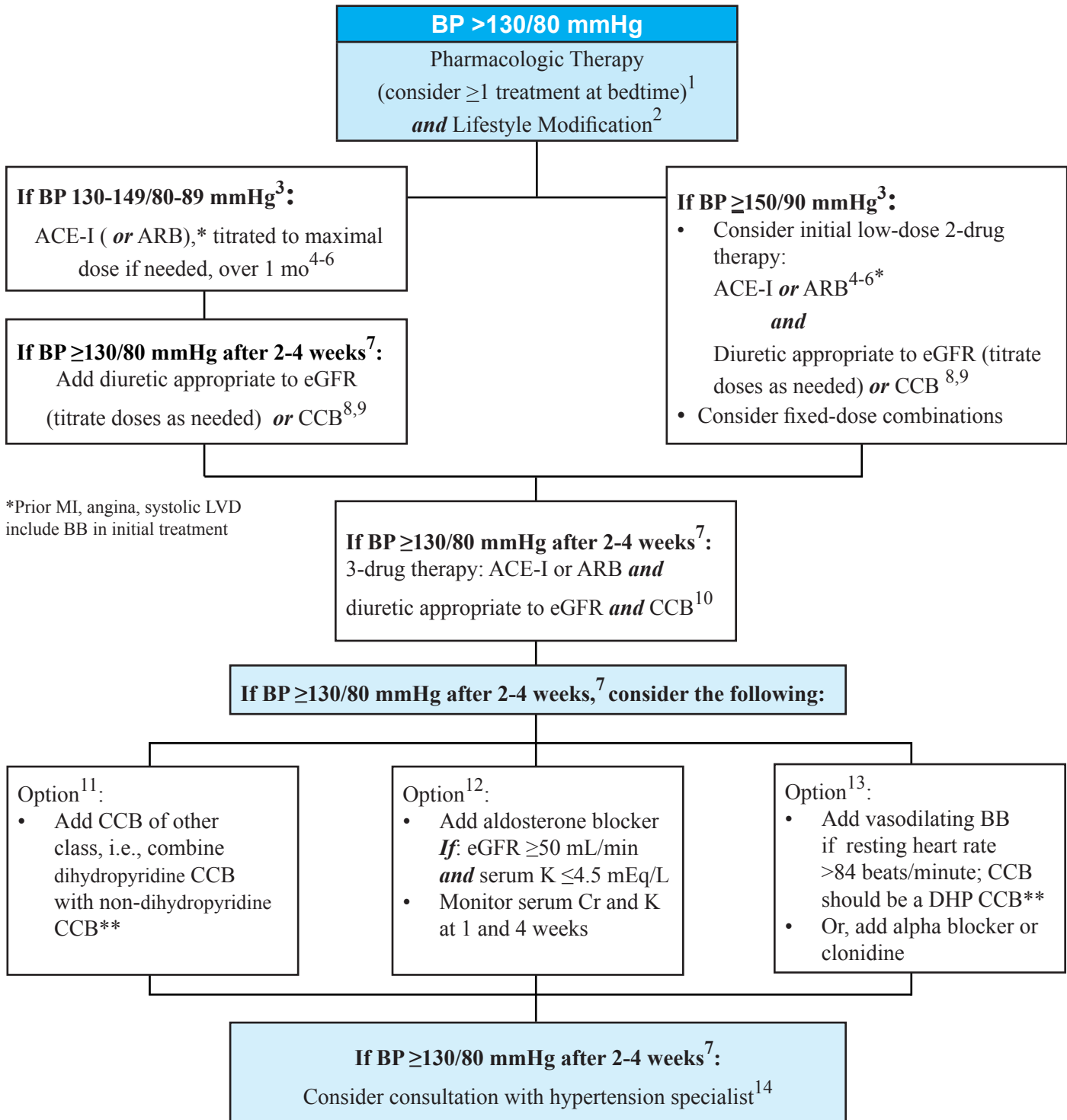
2. However, new 2012 studies provide evidence to support the increasing use of out-of-office BP monitoring in persons with diabetes. A study of ABPM in 12,600 persons with diabetes and hypertension found a prevalence of white-coat hypertension of 33%[3] while another study of 554 persons with diabetes noted prevalences of white-coat hypertension in 20% and of masked hypertension in another 10%.[1] Furthermore, as compared to persons with hypertension only, those with hypertension and diabetes are significantly more likely to have elevated nocturnal BP, the strongest BP predictor of adverse cardiovascular and renal outcomes in hypertensive populations with and without diabetes.[3,4] These new studies further suggest that the current target office BP of 130/80 mmHg for persons with diabetes corresponds to a mean daytime BP from an ABPM study of 130/80 mmHg,[1,4] and with less certainty, to a mean home BP of 130/80 mmHg (based on 7 days of twice-daily readings). Earlier studies previously demonstrated that a target office BP of 140/90 mmHg corresponds to a mean daytime BP of 135/85 mmHg from either an ABPM study or from standardized HBPM for 7 days.[5]

3. The decision as to when to initiate pharmacologic therapy for hypertension in diabetes should reflect whether the patient has "higher risk" diabetes with a BP ≥140/90 mmHg or albuminuria (≥30 mg/g of creatinine) or other target organ damage (TOD); TOD includes clinical CVD, left ventricular hypertrophy (LVH), or an estimated GFR below 60 mL/min/1.73m[2] (calculated from the patient's serum

creatinine, age, sex, and race at www.kidney.org/professionals/kdoqi/gfr_calculator.cfm). "Higher risk" diabetes patients should have a diagnosis of hypertension confirmed by 2 visits ≤ one month apart, at which time simultaneous pharmacologic and lifestyle modification therapy should be initiated; controlling BP to goal within six months in such high risk patients has been shown to reduce cardiovascular disease events by about 25%. "Lower risk" diabetes patients with BP =130-139/80-89, no albuminuria, and no TOD may have a limited 3-month trial of lifestyle modification therapy after which pharmacologic therapy should be initiated if BP remains ≥130/80 mmHg.

References

1. Leitao CB, Rodriques TC, Kramer CK, et al. Which patients with diabetes should undergo ambulatory blood pressure monitoring? *J Hypertens* 2011; 29:236-241.

2. American Association of Clinical Endocrinology Task Force. AACE Diabetes Care Plan Guideline. *Endocrine Practice* 2011; 17(Suppl 2):3-53.

3. Gorostidi M, de la Sierra SA, Gonzalez-Albarran O, et al. Abnormalities in ambulatory blood pressure monitoring in hypertensive patients with diabetes. *Hypertens Res* 2011; 34:1185-1189.

4. 4. Cardeso CR, Leite NC, Muxfeldt ES, and Salles GF. Thresholds of ambulatory blood pressure associated with chronic complications in type 2 diabetes. *Am J Hypertens* 2012; 25:82-88.

5. Pickering TG, Miller NH, Ogedegbe G, et al. Call to action on use and reimbursement for home blood pressure monitoring: a joint scientific statement from the American Heart Association, American Society of Hypertension, and Preventive Cardiovascular Nurses Association. *Hypertension* 2008; 52:1-9.

Management of Hypertension in DM

BP >130/80 mmHg

Pharmacologic Therapy

(consider ≥1 treatment at bedtime)[1]

and Lifestyle Modification[2]

If BP 130-149/80-89 mmHg[3]:

ACE-I (*or* ARB),* titrated to maximal dose if needed, over 1 mo[4-6]

If BP ≥130/80 mmHg after 2-4 weeks[7]:
Add diuretic appropriate to eGFR
(titrate doses as needed) *or* CCB[8,9]

If BP ≥150/90 mmHg[3]:
- Consider initial low-dose 2-drug therapy:
ACE-I *or* ARB[4-6]*
   and
Diuretic appropriate to eGFR (titrate doses as needed) *or* CCB[8,9]
- Consider fixed-dose combinations

*Prior MI, angina, systolic LVD include BB in initial treatment

If BP ≥130/80 mmHg after 2-4 weeks[7]:
3-drug therapy: ACE-I or ARB *and*
diuretic appropriate to eGFR *and* CCB[10]

If BP ≥130/80 mmHg after 2-4 weeks,[7] consider the following:

Option[11]:
- Add CCB of other class, i.e., combine dihydropyridine CCB with non-dihydropyridine CCB**

Option[12]:
- Add aldosterone blocker *If*: eGFR ≥50 mL/min *and* serum K ≤4.5 mEq/L
- Monitor serum Cr and K at 1 and 4 weeks

Option[13]:
- Add vasodilating BB if resting heart rate >84 beats/minute; CCB should be a DHP CCB**
- Or, add alpha blocker or clonidine

If BP ≥130/80 mmHg after 2-4 weeks[7]:

Consider consultation with hypertension specialist[14]

**Dihydropyridines (DHP) include: amlodipine, bepridil, felodipine, isradipine, nicardipine, nifedipine, and nisoldipine.
Non-dihydropyridines (non-DHP) include: diltiazem and verapamil.

Modified From:
Diabetes Care 2012; 35(Suppl 1) and *Journal of Clinical Hypertension* 2008; 10:707

1. The 2012 ADA guideline newly recommends administration of ≥1 antihypertensive agent(s) at bedtime.[1] This recommendation is supported by considerable evidence. 24-hour ABPM studies have demonstrated that in normal subjects mean asleep BP declines by ≥10% relative to mean daytime BP and to levels <120/70 mmHg.[2] Persons whose asleep BP declines to normal levels are often referred to as "dippers," while those whose asleep BP fails to decline by ≥10% or even rises are called "non-dippers." Large, prospective observational studies and systematic reviews using ABPM have consistently shown that the mean asleep BP is a stronger predictor of major cardiovascular events than either the mean daytime or mean 24-hour BP in persons with and without diabetes.[3-5] As a result, non-dippers have a more adverse cardiovascular prognosis than dippers. While 40-50% of patients with uncomplicated hypertension exhibit a non-dipping asleep BP, 50-80% of persons with diabetes, chronic kidney disease, or autonomic nervous system dysfunction appear to have this pattern.[6-8] A recent prospective clinical trial of 2,156 subjects with hypertension randomized them to either receive all of their hypertension medications in the morning or at least one of them at bedtime; all patients had a baseline 24-hour ABPM study and then serial ABPM studies during 5.6 years of follow-up.[9] Bedtime administration of ≥1 antihypertensive medication significantly lowered mean asleep BP and mean 24-hour BP (no change in mean daytime BP) and significantly reduced the prevalence of non-dipping pattern from 62% to 34%. After 5.6 years of follow-up, the bedtime administration of ≥1 antihypertensive medication reduced total cardiovascular events by 61%. There were similar significant reductions in asleep BP, non-dipping pattern, and major cardiovascular events in the subgroup of 448 subjects with hypertension and type 2 diabetes[10] and the subgroup of 661 subjects with hypertension and chronic kidney disease.[11] Each 5 mmHg reduction in asleep systolic BP significantly reduced cardiovascular events by 12% and 14%, respectively, in these two studies.[10,11] Decreasing the asleep BP appears to be the strongest predictor for reducing cardiovascular events in persons with diabetes.[12] Because of nighttime and early morning activation of the renin-angiotensin-aldosterone system, bedtime administration of ACE inhibitors and angiotensin receptor blockers appears to be particularly effective in reducing the prevalence of the non-dipping pattern.[13] Based on these data, the 2011 American Association of Clinical Endocrinologists Diabetes Comprehensive Care Plan now suggests consideration of an annual ABPM study to assess hypertension control in patients with hypertension and diabetes.[14] The ADA 2012 guideline appears to suggest the empiric administration of ≥1 antihypertensive agent(s) at bedtime.[1]

2. Comprehensive lifestyle modification may lower BP 5-7/3-5 mmHg. The expected BP reductions from single interventions (note that combined interventions are not fully additive) are listed in parentheses: weight loss (1/1 mmHg/kg lost); restriction of dietary sodium to 1500-2300 mg/day (5/3 mmHg); the Dietary Approaches to Stop Hypertension (DASH) diet (10/5 mmHg). Note: DASH is a high-potassium diet to be avoided if eGFR is <60 mL/min to minimize hyperkalemia risk; moderate aerobic exercise such as walking or cycling for 30-45 minutes on 5-7 days/week (4/3 mmHg). Note: Avoid walking programs if peripheral neuropathy is significant; restriction of alcohol to ≤2 drinks/day in men and ≤1 drink/day in women (3/2 mmHg).

3. Most hypertensive patients with diabetes require ≥3 drugs to bring BP below 130/80 mmHg; patients with eGFR <60 mL/min require an average of 4 drugs. If baseline BP is ≥20/10 mmHg above goal, consider initial low-dose two-drug therapy rather than monotherapy except for frail, elderly patients or those with

substantial orthostatic BP changes. Initial low-dose two drug therapy provides a greater and more rapid BP reduction, may improve patient adherence and reduce clinician inertia, and thereby improve hypertension control rates.

4. An evidence-based pharmacologic regimen for hypertension in diabetes has not been determined. Similar reductions in cardiovascular events have been demonstrated for ACE inhibitors (ACE-Is), angiotensin receptor blockers (ARBs), thiazide-type diuretics, and calcium channel blockers (CCBs). Compared to other agents, beta blockers (BBs) may reduce the risk of stroke less effectively in persons over age 60 years, while alpha-blockers less effectively reduce stroke and heart failure. ACE-Is and ARBs slow nephropathy progression and loss of GFR more effectively than other agents in diabetic patients with macroalbuminuria (≥300 mg/gram creatinine) and eGFR <60 mL/min, but have not yet been shown to slow the loss of GFR in patients with normoalbuminuria or microalbuminuria. Recent studies indicate that ACE-Is and ARBs may help to prevent the development and slow the progression of mild to moderate nonproliferative retinopathy independent of BP lowering. ACE-Is or ARBs should be included as initial hypertensive therapy in most hypertensive patients with diabetes. Doses may be titrated to maximal dose over one month, if needed, to achieve goal BP. In patients with macroalbuminuria and eGFR <60 mL/min, ACE-I or ARB doses should be titrated to the target levels used in clinical studies (see table next column), if tolerated by serum potassium and creatinine levels. In the presence of renal insufficiency, ACE-Is and ARBs may significantly increase serum potassium and/or creatinine which should therefore be monitored within one to two weeks and again in 4 weeks following the initiation or upward titration of these drugs. A serum potassium over 5.4 mmol/L or a persistent reduction in renal function >30% may require discontinuation

of therapy or a reduction in dose. The renoprotective effect of ACE-Is and ARBs may be lost or muted as serum creatinine rises to >3.0 mg/dL.

Titrate ACE-I/ARB to study dose in CKD (if tolerated):	
ACE-I (mg/d)	ARB (mg/d)
Lisinopril, 20-40	Candesartan, 16-32
Benazepril, 30-40	Irbesartan, 300
Ramipril, 10-20	Telmisartan, 80
Perindopril, 4-16	Valsartan, 160-320
Trandolapril, 3-4	Losartan, 100

Table 1: Goal Doses for ACE inhibitors and Angiotensin Receptor Blockers for Hypertension Management in Diabetes [*Am J Kid Disease* 2004; 43(May Suppl):S142]

5. If the patient has had a prior myocardial infarction, active angina, or systolic left ventricular (LV) dysfunction, a beta-blocker (BB) should be added to the ACE inhibitor or ARB as part of the initial treatment regimen.

6. If ACE-Is and ARBs are not tolerated, substitute a diuretic or CCB (verapamil or diltiazem) as initial therapy as long as there is no proteinuria.

7. The antihypertensive regimen should be adjusted at intervals no longer than every two to four weeks until goal BP is achieved. Recent studies suggest that two-week encounter intervals may result in a more rapid reduction in BP and achievement of goal BP.

8. If BP remains above goal on ACE-I or ARB therapy, either a diuretic appropriate to the patient's GFR or a CCB can be added. In the diabetes subgroup of the 2008 ACCOMPLISH clinical trial, a regimen based on benazepril and amlodipine reduced cardiovascular events by 21% compared to a regimen based on benazepril and hydrochlorothiazide.

9. Thiazide diuretics (hydrochlorothiazide, 12.5-50 mg/day, or chlorthalidone, 12.5-25 mg/day—the latter lowers BP more effectively) are excellent second-step agents except in patients with

refractory gout, thiazide-induced hyponatremia, or eGFR <30 mL/min. In patients with eGFR <30 mL/min, short-acting loop diuretics (furosemide or bumetanide) administered twice daily or the long-acting loop diuretic, torsemide, administered once daily, may be substituted for the less effective thiazides. In general, the dose of loop diuretic should be carefully titrated in patients with eGFR <30 mL/min. If a short-acting loop diuretic is administered, the second daily dose should be administered no later than 4 PM to avoid nocturia. Serum potassium and creatinine should be monitored after one week, after two to four weeks, and thereafter at frequent intervals following initiation or dose increments of these drugs because of the risk of hyperkalemia and renal insufficiency with these medications.

10. Extended-release formulations of verapamil (180-480 mg/day) or diltiazem (180-360 mg/day) are favored third-step agents in preference to dihydropyridine (DHP) CCBs (e.g., amlodipine or extended-release nifedipine) as the non-DHP CCBs more consistently reduce albuminuria. However, DHP CCBs are acceptable alternatives as long as an ACE inhibitor or ARB is a component of the therapeutic regimen; DHP CCBs are preferred in the presence of bradycardia, systolic LV dysfunction, or concurrent beta-blocker therapy. The addition of BBs to ACE-Is or ARBs often does not result in a substantial BP reduction unless the resting heart rate is >84 beats per minute.

11. Many patients with diabetes and hypertension will require four drugs to lower BP below 130/80 mmHg. Selection of a fourth-step agent must be based on clinical judgment as comparative clinical trials among agents are not available. For patients whose eGFR is ≥50 mL/min and baseline serum potassium is ≤4.5 mmol/L, addition and subsequent titration of an aldosterone blocker such as spironolactone, 12.5-50 mg/day, or eplerenone 50-100 mg/day, may effectively lower systolic BP by 15-

30 mmHg. Serum potassium and creatinine should be monitored after one week, after two to four weeks, and thereafter at frequent intervals following initiation or dose increments of these drugs because of the risk of hyperkalemia and renal insufficiency with these medications.

12. In patients for whom aldosterone blockers are contraindicated or not tolerated, combining a DHP CCB with verapamil or diltiazem may lower BP by 10/10 mmHg. This regimen may be complicated by peripheral edema in 20% of patients.

13. Another fourth-step option is to substitute a DHP CCB for any verapamil or diltiazem therapy, and then add a BB drug. This regimen may lower BP in patients who have a relatively elevated heart rate above 84 beats/minute. BBs should generally not be added to verapamil or diltiazem because of the risk of bradycardia. In contrast to other BBs, the vasodilating BBs carvedilol and nebivolol are less likely to aggravate glycemic and lipid control or increase weight. Carvedilol also reduces albuminuria to a greater extent than metoprolol, although the generic formulation must be administered twice daily. Consideration may also be given to other agents as fourth- or fifth-step therapy: alpha blockers such as doxazosin or terazosin or transdermal or oral clonidine may be effective therapy for some patients. The role of the direct renin inhibitor, aliskiren, in the management of diabetic hypertension has not yet been fully ascertained. In recent clinical trials, combining ACE-Is with ARBs did not lower BP meaningfully, did not further reduce CVD or renal events, but did significantly increase side effects; therefore, this combination should generally be avoided. A role for combining ACE-Is and ARBs in patients with macroalbuminuria and eGFR <60 mL/min is currently under investigation.

14. Patients with difficult-to-control hypertension should be regularly reassessed for poor adherence to pharmacologic therapy and

lifestyle modification. Poor adherence may result from inadequate patient education, cost issues, unrecognized medication side effects, and complex therapeutic regimens. Out-of-office BP measurement with home BP monitoring, if not already performed, should be considered to rule out "white coat"-resistant hypertension. Referral to a hypertension specialist may be helpful, especially for evaluation of secondary causes of hypertension.
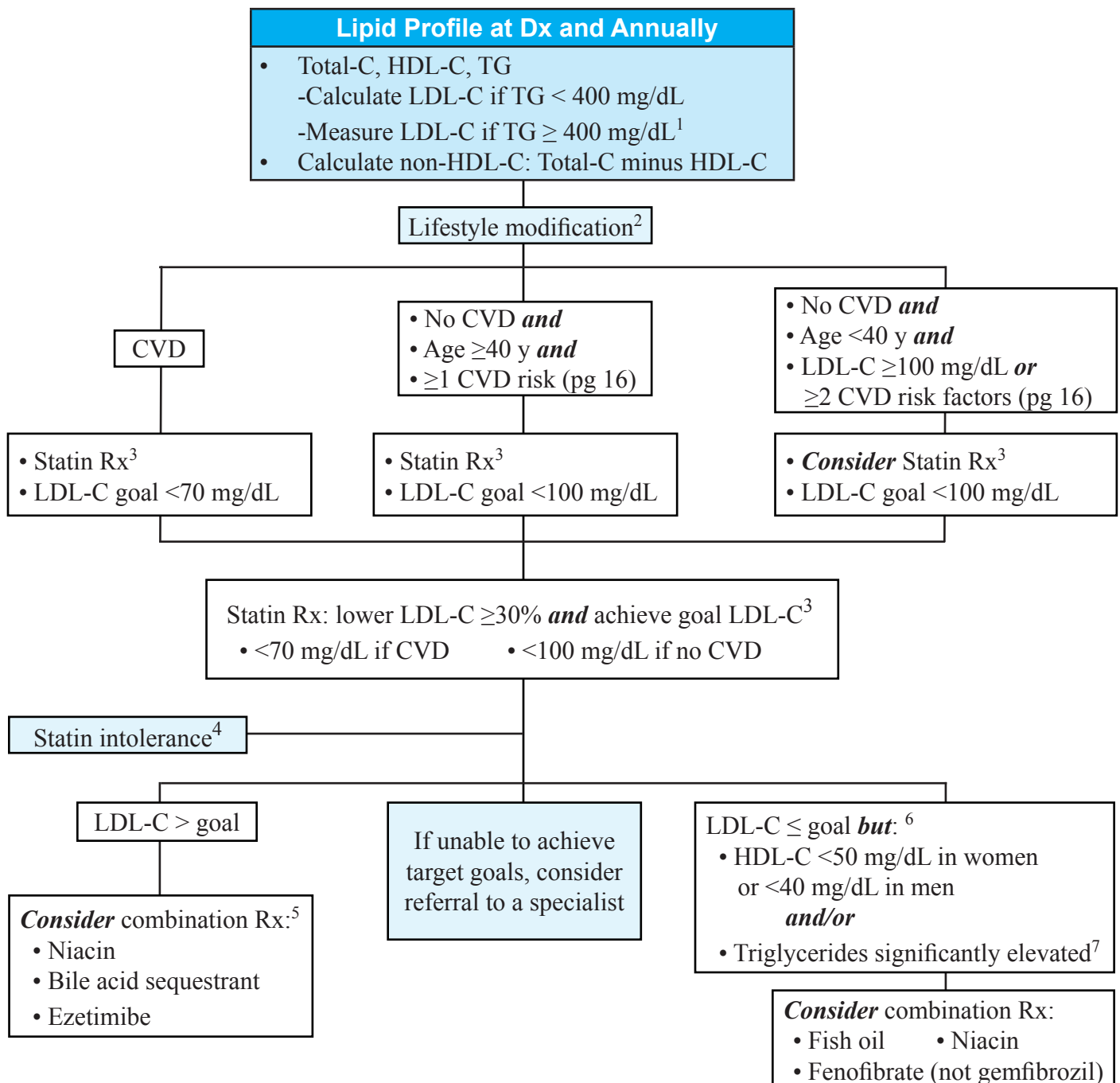
References

1. American Diabetes Association. Standards of medical care in diabetes – 2012. *Diabetes Care* 2012; 35(Suppl 1): S11-S63.

2. Pickering TC, Hall JE, Appel LJ, et al. AHA Scientific Statement: recommendations for blood pressure measurement in humans. *Hypertension* 2005; 45:142-161.

3. Fan HQ, Li Y, Thijs L, et al. International Database on Ambulatory Blood Pressure in Relation to Cardiovascular Outcomes Investigators: Prognostic value of isolated nocturnal hypertension on ambulatory measurement in 8711 individuals from 10 populations. *J Hypertens* 2010; 28:2036-2045.

4. Hansen TW, Li Y, Boggia J, et al. Predictive role of nighttime blood pressure. *Hypertension* 2011; 57:3-10.

5. Eguchi K, Pickering TG, Hoshide S, et al. Ambulatory blood pressure is a better marker than clinic blood pressure in predicting cardiovascular events in patients with/without type 2 diabetes. *Am J Hypertens* 2008; 21:443-450.

6. Hermida RC, Calvo C, Ayala D, et al. Relationship between physical activity and blood pressure in dipper and non-dipper hypertensive patients. *J Hypertens* 2002; 20:1097-1104.

7. Gorostidi M, de la Sierra A, Gonzalez-Albarran O, et al. Abnormalities in ambulatory blood pressure in hypertensive patients with diabetes. *Hypertens Res* 2011; 34:1185-1189.

8. Minutolo R, Agarwal R, Borrelli S, et al. Prognostic role of ambulatory blood pressure measurement in patients with non-dialysis kidney disease. *Arch Intern Med* 2011; 171:1090-1098.

9. Hermida RC, Ayala DE, Mojon A, Fernandez JR. Influence of circadian time of hypertension treatment on cardiovascular risk: results of the MAPEC study. *Chronobiol Int* 2010; 27:1629-1651.

10. Hermida RC, Ayala DE, Mojon A, Fernandez JR. Influence of time of day of blood pressure-lowering treatment on cardiovascular risk in hypertensive patients with type 2 diabetes. *Diabetes Care* 2011; 34:1270-1276.

11. Hermida RC, Ayala DE, Mojon A, Fernandez JR. Bedtime dosing of antihypertensive medications reduces cardiovascular risk in CKD. *J Am Soc Nephrol* 2011; 22:2313-2321.

12. Hermida RC, Ayala DE, Mojon A, Fernandez JR. Sleep-time blood pressure as a therapeutic target for cardiovascular risk reduction in type 2 diabetes. *Am J Hypertens* 2012; 25:325-334.

13. Hermida RC, Ayala DE, Fernandez JR, et al. Circadian rhythms in blood pressure regulation and optimization of hypertension treatment with ACE inhibitor and ARB medications. *Am J Hypertens* 2011; 24:383-391.

14. American Association of Clinical Endocrinology Task Force. AACE Diabetes Care Plan Guideline. *Endocrine Practice* 2011; 17(Suppl 2):3-53.

Dyslipidemia in Diabetes

Dylispidemia is a major contributor to cardiovascular disease (CVD) risk in diabetes, and its effective treatment reduces macrovascular complications and mortality. Compared to the general population, persons with diabetes have similar levels of LDL-cholesterol; LDL-particles that are smaller, more dense, and more atherogenic; and twice the frequency of low HDL-cholesterol and elevated triglycerides (TG). LDL-C is the primary lipid determinant of CVD risk, but low HDL-C and elevated TG also predict CVD events. As a result, the non-HDL-cholesterol level [total cholesterol (Total-C) minus HDL-C] is a better predictor of CVD risk. Non-HDL-C goals are 30 mg/dL higher than the LDL-C goals listed in the algorithm for management of dyslipidemia.

Lipid Profile at Dx and Annually

- Total-C, HDL-C, TG
  - Calculate LDL-C if TG < 400 mg/dL
  - Measure LDL-C if TG ≥ 400 mg/dL[1]
- Calculate non-HDL-C: Total-C minus HDL-C

↓

Lifestyle modification[2]

CVD

- Statin Rx[3]
- LDL-C goal <70 mg/dL

- No CVD **and**
- Age ≥40 y **and**
- ≥1 CVD risk (pg 16)

- Statin Rx[3]
- LDL-C goal <100 mg/dL

- No CVD **and**
- Age <40 y **and**
- LDL-C ≥100 mg/dL **or**
  ≥2 CVD risk factors (pg 16)

- **Consider** Statin Rx[3]
- LDL-C goal <100 mg/dL

↓

Statin Rx: lower LDL-C ≥30% **and** achieve goal LDL-C[3]
- <70 mg/dL if CVD   • <100 mg/dL if no CVD

↓

Statin intolerance[4]

LDL-C > goal

Consider combination Rx:[5]
- Niacin
- Bile acid sequestrant
- Ezetimibe

If unable to achieve target goals, consider referral to a specialist

---

LDL-C ≤ goal **but**: [6]
- HDL-C <50 mg/dL in women
  or <40 mg/dL in men
  and/or
- Triglycerides significantly elevated[7]

Consider combination Rx:
- Fish oil   • Niacin
- Fenofibrate (not gemfibrozil)

Annotations

1. When TG are ≥400 mg/dL, calculation of the LDL-C level is inaccurate, and LDL-C must be measured directly.

2. Lifestyle modification is useful for all patients with diabetes but is rarely sufficient to optimize dyslipidemia. LDL-C can be lowered 6-8% by reducing saturated and trans-fat and cholesterol, potentially another 15% by adding foods that lower LDL-C (plant sterols/stanols, soluble fiber, nuts, and possibly soy protein), and by 5-8% with a 10-lb weight loss. Triglycerides may be lowered by weight loss, restriction of simple sugars and alcohol, utilization of a low-fat diet in which saturated fats are replaced with monounsaturated fats, and by improved glycemic control. HDL-C may be increased by weight loss, aerobic exercise, and smoking cessation.

3. Irrespective of baseline LDL-C level or the presence of CVD risk factors or CVD, lowering LDL-C by 80-120 mg/dL with statins may reduce major CVD events by 40-50% in persons with diabetes. Statin therapy is therefore recommended or should be considered for most persons with diabetes. Because most statin studies lowered LDL-C ≥30% *and* below 100 mg/dL, *both* of these goals should be accomplished, if possible; in the presence of CVD, it is reasonable to pursue an LDL-C goal <70 mg/dL. The table "Medications for Lipid Control" (page 27) lists the lowest statin doses that reduce LDL-C ≥30% along with the maximal daily doses and mean expected percent reduction in LDL-C for different statins; each doubling of statin dose above the listed standard dose lowers LDL-C by an additional 6%.

4. Statin intolerance may occur in 5-10% of persons, most often due to myalgias. Treatment options include: (1) a trial of a different statin, particularly fluvastatin, pravastatin, or rosuvastatin; (2) rosuvastatin therapy 1-3 times/week; (3) gemfibrozil reduces CVD events in persons with diabetes in whom HDL-C is low and/or triglycerides are elevated but who have minimal LDL-C elevation; (4) niacin, often in combination with (5) bile acid sequestrants and/or (6) ezetimibe. Regimens 1, 2, and 4 may lower LDL-C by 20-30%. Data showing that ezetimibe improves CVD outcomes are not available.

5. If maximal doses of a potent statin do not lower LDL-C to goal, additional therapy to lower LDL-C may be *considered*. Niacin and bile acid sequestrants can lower LDL-C by 10-15%; as monotherapy, each has been demonstrated to reduce CVD events. Ezetimibe lowers LDL-C 15-20%, but CVD outcome data are not available.

6. Once LDL-C has been optimized, combination therapy with niacin, fenofibrate (but not gemfibrozil due to an interaction with statins), or fish oil may be *considered* to lower persistently elevated triglycerides and/or raise low HDL-C. Combination therapy has not yet been shown to safely reduce CVD events in randomized trials. Two clinical trials of statins combined with niacin are in progress. The recent ACCORD trial found that the addition of fenofibrate to simvastatin did not reduce major CVD events; subgroup analysis of this trial found a possible benefit of fenofibrate in patients with triglycerides ≥204 mg/dL and HDL-cholesterol <35 mg/dL. If combination therapy is selected, doses of niacin, fenofibrate, or fish oil should be adjusted to target a non-HDL-C level <100 mg/dL in persons with CVD and <130 mg/dL in persons with no CVD.

7. Patients with triglycerides ≥1000 mg/dL should be treated promptly with a fibrate or niacin to reduce the risk of acute pancreatitis. Fish oil, 3-9 g/day, may be added if necessary.

Medications for Lipid Control

Medication	Dose	LDL Reduction	HDL Elevation	TG Reduction	Ave. Cost/Mo.*	Comments
Rosuvastatin	5 mg	45%	13%	35%	$157	
Rosuvastatin[1]	40 mg	63%	10%	28%	$157	
Atorvastatin[2]	10 mg	39%	6%	19%	$122	
Atorvastatin[3]	80 mg	60%	5%	37%	$173	
Simvastatin[4]	20 mg	35%	8%	19%	$4	
Lovastatin[5]	40 mg	30%	7%	14%	$5	
Pravastatin[6]	40 mg	32%	7%	21%	$5	
Pitavastatin	4mg	45%	5%	19%	$119	
Fenofibrate[7]	145 mg or 160 mg	Variable	15-23%	36-55%	$54	Should not be used with renal disease.
Niacin[8]	2000 mg	10-20%	20-35%	30-70%	$10	4 X 500 mg
Niaspan[9]	2000 mg	17%	26%	35%	$303	2 X 100 mg
Ezetimibe	10 mg	15-20%	0-1%	2-8%	$131	Lower numbers represent add-on to statin therapy; higher numbers represent monotherapy. HDL was noted to decrease in the ARBITER-6 trial
Colesevelam	4.5 g	18%	3%	9%	$247	Welchol TM 7 tablets/day (6 X 625 mg; $1.37 per tab)
Cholysteramine[10]	12 g (3 packets)	20%		11%	$21	Take 1 hr after or 4 hr before other meds ($0.07 per 4 g pack)

NOTE: Medication selected should decrease LDL by at least 30%.
LDL, HDL, and triglyceride numbers represent mean drug effect as reported by package insert.

1 JUPITER trial (20 mg) *N Engl J Med* 2008;359:2195-207.
2 ASCOT trial *Lancet*. 2003 Apr 5;361(9364):1149-58 and CARDS *Lancet*. 2004 Aug 21-27;364(9435):685-96.
3 PROVE-IT *J Am Coll Cardiol*. 2005 Oct 18;46(8):1405-10 and TNT *N Engl J Med*. 2005 Apr 7;352(14):1425-35
4 Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III Guidelines Grundy, S, Cleeman, J, Merz CNB, Brewer, HB, Clark, L, Hunninghake, D, Pasternak, R., Smith, S, Stone, N. *Circulation*. 2004;110:227-239.
5 AFCAPS *JAMA*. 1998 May 27;279(20):1615-22.
6 WOS trial: *N Engl J Med* 1995;333:1301-7, LIPID trial: *N Engl J Med* 1998;339:1349-1357, CARE trial: *N Engl J Med* 1996;335:1001-9.
7 FIELD study *Lancet*. 2005 Nov 26;366(9500):1849-61.
8 Coronary Drug Project *J Am Coll Cardiol*. 1986 Dec;8(6):1245-55 and HATS study *N Engl J Med*. 2001 Nov 29; 45(22):1583-92 and FATS *NEJM* 1990; 323:1289-98.
9 ARBITER 2 *Circulation*. 2004 Dec 7;110(23):3512-7 and ARBITER 6 *J Am Coll Cardiol*. 2010 Jun 15;55(24):2721-6
10 Lipid Research Clinics, *JAMA* 1984; 251:351-374.
*Cost data per January 2011 AWP or MAC, where available.

Diabetes Foot Care:
Risk Assessment & Management

Persons with diabetes have a 25% lifetime risk of developing a foot ulcer. These foot ulcers progress to osteomyelitis and/or to lower extremity amputation in 15-20% of cases at a cost of $27 billion/year. This will lead to a lifetime of significant disability.

Multiple factors contribute to the pathogenesis of diabetic foot ulcers:

- **Sensory neuropathy** results in a loss of protective sensation (LOPS) in the feet with subsequent callus formation and failure to recognize traumatic injury to the feet (e.g., mechanical trauma from ill-fitting shoes). Callus and LOPS can lead to subcutaneous hemorrhage beneath the callus—a "pre-ulcer"—and subsequent ulceration if pressure is not relieved promptly.

- **Motor neuropathy** results in atrophy of the intrinsic muscles of the feet and secondary foot deformities which become sites for callus formation and subsequent ulceration.

- **Autonomic neuropathy** results in reduced sweating of the feet. The resulting dry skin may accelerate callus formation and/or may fissure, leading to a foot ulcer.

- **Peripheral arterial disease** impairs the healing of foot ulcers and facilitates secondary infections. Subsequent deep soft tissue infection may lead to osteomyelitis and amputation.

- **Reduced visual acuity and/or obesity and generalized debility** may prevent patients from seeing or reaching their feet, thereby impairing self-care and early detection of foot lesions. Up to 40-50% of diabetic patients cannot see and/or reach their feet.

- **Nephropathy** increases the risk of diabetes foot ulceration for uncertain reasons.

- **Major depression** is associated with a two-fold increased risk of a first foot ulceration.

Fortunately, comprehensive foot care programs can reduce foot ulcer and subsequent amputation rates by at least 50% and may even be a cost-saving intervention. Essential components of these programs include:

1. Identifying patients at increased risk for foot ulcer with frequent comprehensive foot evaluation.

2. Educating and motivating patients at increased risk to regularly care for their feet (see Appendix J: Taking Care of Your Feet). Effective education may require the services of a podiatrist or diabetes educator (Appendix A). Additional basic foot care patient education can be found at www.ndep.nih.gov/diabetes/pubs/FootTips.pdf and https://diabetes.niddk.nih.gov/dm/pubs/complications_feet

3. Referring patients at increased risk of complications to podiatrists for prophylactic nail and skin care and provision of therapeutic footwear (socks, insoles, special shoes) when indicated, with frequency of podiatry follow-up determined by individual level of risk.

4. Detecting foot problems early by daily patient self-inspection (which may require the assistance of another person) and by inspection of the feet at every office visit in persons at increased risk of foot ulcer.

Patients at increased risk for foot ulceration can be identified and then risk-stratified by considering two historical features and four exam components. Risk stratification defines annual ulcer risk and determines management strategies (see Table 1 on next page).

Table 1: Foot Ulcer Risk Management					
Risk Level	Definition	% Ulcer per Year	Education	Visual Inspection	Podiatry
3	Prior amputation or ulcer	20-30 %	Diabetes educator Test knowledge	q visit	q 1-2 mo Insoles ± shoe gear; Vasc Surg if PAD
2	PAD ± LOPS	6%	Diabetes educator Test knowledge	q visit	q 2-3 mo Insoles ± shoe gear; Vasc Surg if PAD
1	LOPS ± Deformity	4%	Enhanced patient education Footwear advice	q visit	q 3-6 mo Insoles ± shoe gear
0	No LOPS, PAD, or deformity	<2%	Basic patient education	Annual exam*	Not needed
Diabetes Care: 2008 31:1679					*see appendix D

Important Components of Risk:

- **Prior amputation**

- **Prior foot ulcer**

- **Peripheral arterial disease (PAD):** absence of both dorsalis pedis *and* posterior tibial pulses on one or both feet

- **Foot deformities:** hammer toes, claw toes, prominent metatarsal heads, bunions, overlapping toes or a collapsed plantar arch (Charcot foot)

- **Loss of protective sensation (LOPS):** protective sensation is considered intact *if* patients accurately sense pressure from the Semmes-Weinstein 5.07/10g monofilament (MF) *and* have a normal response to one of the three following tests. There are no consensus recommendations on how to best perform these sensory exams. Approaches suggested by the ADA and/or International Working Group on the Diabetic Foot are included below:

  Vibratory sensation testing may be the most sensitive of the three tests.
  - 128 Hz tuning fork (TF)—see the adjacent panel for a suggested technique.
  - Vibration perception threshold testing with a biothesiometer:
    - Place on pulp of great toe
    - Patient detects the mean of 3 readings ≤25 volts

  Ankle reflexes
  - Sensate: reflexes present without/with reinforcement

  Pin prick sensation
  - Apply disposable pin proximal to nail of great toe
  - Sensate: senses pressure sufficient to deform skin

  Patients with ≥1 abnormal sensory test have LOPS.

Detect LOPS: Vibration Sense

1. Patient closes eyes
2. Apply 128Hz TF to wrist
3. Ask pt to distinguish vibration from pressure so pt knows what to expect
4. Apply TF perpendicularly to dorsum of great toe proximal to nail bed
5. Apply TF 3 times to each great toe: 2 times with vibration, one time with pressure
6. Ask the pt: "Pressure or vibration?"
7. Sensate: Correctly identifies ≥2/3 applications

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Visual Inspection and Annual Comprehensive Foot Exam

See Appendix D: Comprehensive Foot Examination for a potential format for documenting care. Evaluate for:

• Signs of excess foot pressure: persistent erythema after shoe removal, callus, callus with subcutaneous hemorrhage ("pre-ulcer" requiring urgent podiatry referral);

• Dry skin and fissuring from autonomic neuropathy;
• Poor self-care: nail pathology, interdigital maceration with fungal infection;
• Proper footwear.

Right Foot   **Left Foot**
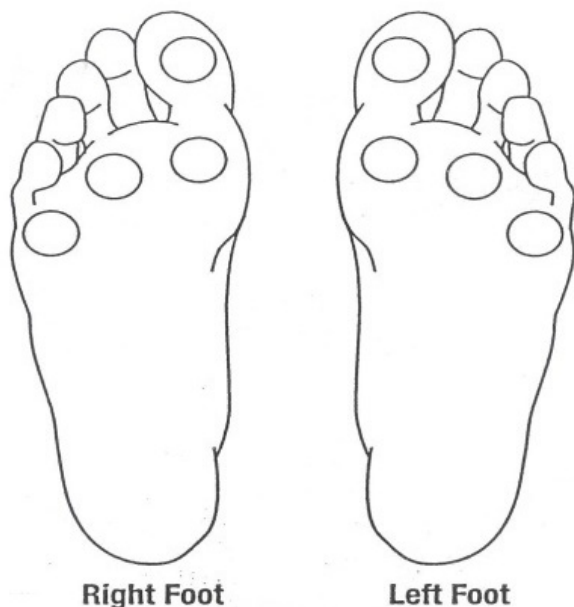
Using the 5.07/10g MF
1. Demonstrate sensation on the forearm or hand.
2. Place monofilament perpendicular to test site.
3. Bow into C-shape for one second.
4. Test 4 sites/foot: Predicts 95% of ulcer formers vs. 8 sites
   • Heel testing does not discriminate ulcer formers
   • Avoid calluses, scars, and ulcers
5. Minimize bias
   • Test sites in random sequence
   • Test each site 3X
   • Sham test as 1 of 3
6. Ask "Do you feel it? Yes or no?"
7. Retest site if patient fails (misses 2/3 of responses).

Key Points
• Insensate at 1 site = insensate feet
• Pt may be falsely insensate due to edema, cold feet
• Test annually when sensation normal
• Use monofilament <100X per day; replace if bent
• Use calibrated monofilament

Photo courtesy of Dr. Scott Clark, DPM

Diabetic Nephropathy

Referral for Nephrology Consultation

The National Kidney Foundation and the American Diabetes Association support referral for nephrology consultation at an eGFR of less than or equal to 30 mL/min (CKD IV); consultation with a nephrologist has been found to reduce cost, improve quality of care, and delay the time to initiation of dialysis (1,14,15). Patients may benefit from nephrology consultation for refractory hypertension (see Appendix E: CKD Assessment Algorithm), persistent nephrotic syndrome on RAAS inhibition, rapidly worsening renal failure, hematuria/active urinary sediment, or any other atypical clinical features of alternate explanation for CKD other than DM.
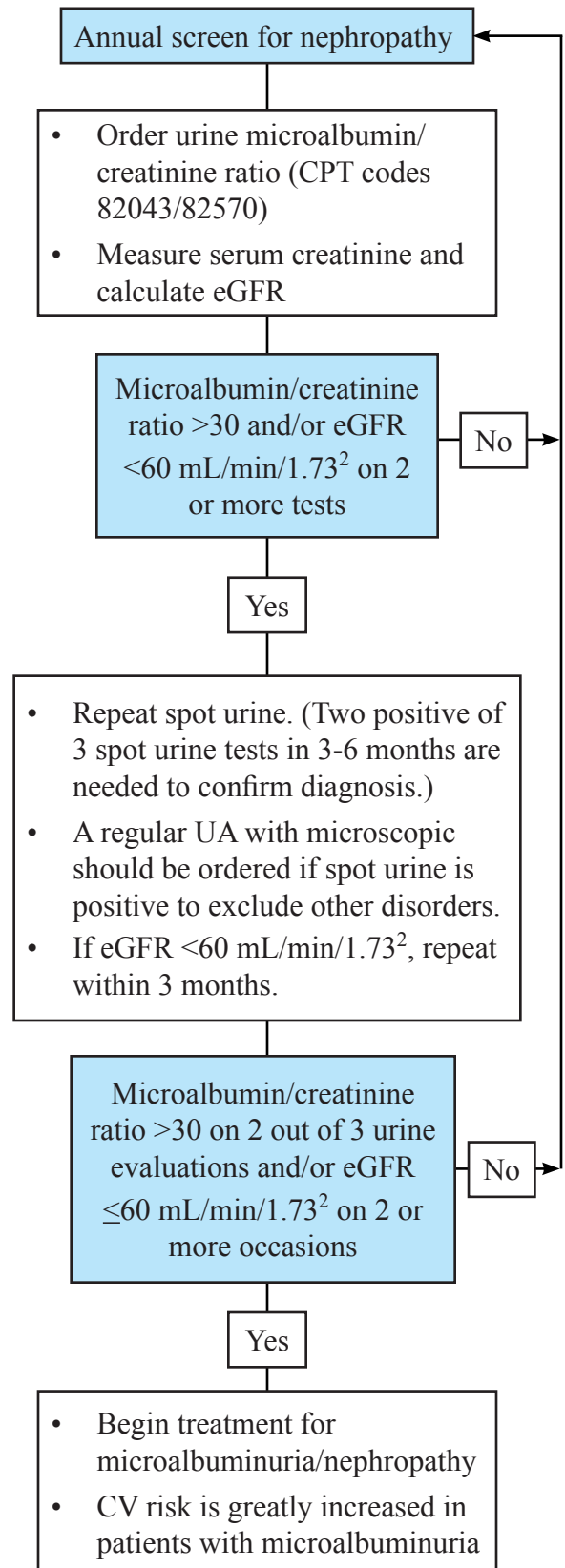
RAAS Inhibition

Renin-angiotensin-aldosterone system (RAAS) inhibition, ACE or ARB class, is equally effective in the treatment of both type 1 and 2 diabetic nephropathy. Preliminary evidence suggests dual RAAS blockage with combined ACE/ARB inhibition offers greater short term benefits in terms of synergism in blood pressure and proteinuria reduction (3), but with more complications, especially hyperkalemia (7). Whether this, or the use or combination of ACE/ARB inhibition with direct renin inhibitors, proves to be effective long-term renoprotection is unknown and is not recommended.

There are no long term data regarding the benefit of the combination of ACE, ARB, direct renin inhibition, or aldosterone blockade in slowing the rate of decline of GFR in diabetic patients.

Please refer to Diabetes and Hypertension (pgs. 18-24). RAAS inhibition is preferred when appropriate; additions or changes in medications should be followed with timely lab monitoring (one to two weeks) for hyperkalemia/ARF. BP targets are $\leq$130/80 mmHg, or $\leq$120/75 mmHg if proteinuric (greater than 500-1000 mg/day) (4).

Often at least 3 agents, and especially a diuretic, will need to be used to meet these goals.

Annual screen for nephropathy

- Order urine microalbumin/ creatinine ratio (CPT codes 82043/82570)
- Measure serum creatinine and calculate eGFR

Microalbumin/creatinine ratio >30 and/or eGFR <60 mL/min/1.73^2 on 2 or more tests

No

Yes

- Repeat spot urine. (Two positive of 3 spot urine tests in 3-6 months are needed to confirm diagnosis.)
- A regular UA with microscopic should be ordered if spot urine is positive to exclude other disorders.
- If eGFR <60 mL/min/1.73^2, repeat within 3 months.

Microalbumin/creatinine ratio >30 on 2 out of 3 urine evaluations and/or eGFR $\leq$60 mL/min/1.73^2 on 2 or more occasions

No

Yes

- Begin treatment for microalbuminuria/nephropathy
- CV risk is greatly increased in patients with microalbuminuria

Albuminuria and Proteinuria

Screening for kidney disease should begin 5 years after the diagnosis of type 1 diabetes and at the diagnosis of type 2 diabetes. Albuminuria reduction may be considered a treatment target in diabetic nephropathy. Hypertensive patients with albuminuria should be treated with ACE/ARB. Treatment with an ACE/ARB may be considered in normotensive patients with albuminuria (2).

Attempts should be made to lower proteinuria to 500-1000 mg daily (2,4,6). If the proteinuria goal is not met with the addition and maximization of ACE/ARB therapy, a nondihydropyridine calcium channel blocker may be used if the patient is not already on a beta blocker (13).

Multiple studies show reduction in macroalbuminuria and the decline of renal function in these patients with use of RAAS inhibitors. In addition, best evidence suggests usage of ACE-I in persons with type 1 DM with any degree of albuminuria or ARB in patients with type 2 DM with microalbuminuria provides benefit. Although there is not current evidence to show that RAS blockers prevent GFR loss in microalbuminuria, they prevent retinopathy and lower blood pressure effectively (refer to Hypertension Treatment). In addition, ACE/ARB may be used in patients with type 2 DM and CKD and macroalbuminuria (8, 9, 10, 11, 14, 16, 17, 18, 19, 20, 21, 22).

Protein Restriction

Given other dietary restrictions in the treatment of DM, the role of protein restriction is uncertain or additive to other measures (BP and glycemic control, ACE/ARB inhibition). A moderate protein restriction to 0.8-1 g/kg day may be reasonable (12).

References

1. National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. *Am J Kidney Dis* 39:S1-S266, 2002 (suppl 1).

2. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. *Am J Kidney Dis* 49: S1-S180, 2007 (suppl 2)

3. Morgensen CE, et. al. Randomized controlled trial of dual blockade of the renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. *BMJ* 2000; 321 1440-1444.

4. National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. *Am J Kidney Disease* 43: S1-S290, 2004, (suppl 1).

5. Messerli FH, Mancia G, Conti CR, Hewkin AC, Kupfer S, Champion A, Kolloch R, Benetos A, Pepine CJ. Dogma disputed: can aggressively lowering blood pressure in hypertensive patients with coronary artery disease be dangerous? *Ann Intern Med* 2006 Jun 20;144(12):884-93.

6. Gross JL, de Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: diagnosis, prevention, and treatment. *Diabetes Care* 2005 Jan;28(1):164-76.

7. Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, Schumacher H, Dagenais G, Sleight P, Anderson C. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med*. 2008 Apr 10;358(15):1547-59. Epub 2008 Mar 31.

8. de Zeeuw D, Remuzzi G, Parving HH, Keane WF, Zhang Z, Shahinfar S, Snapinn S, Cooper ME, Mitch WE, Brenner BM. Proteinuria, a target for renoprotection in patients with type 2 diabetic nephropathy: lessons from RENAAL. *Kidney Int* 2004 Jun;65(6):2309-20.

9. Pohl MA, Blumenthal S, Cordonnier DJ, De Alvaro F, Deferrari G, Eisner G, Esmatjes E, Gilbert RE, Hunsicker LG, de Faria JB, Mangili R, Moore J Jr, Reisin E, Ritz E, Schernthaner G, Spitalewitz S, Tindall H, Rodby RA, Lewis EJ. Independent and additive impact of blood pressure control and angiotensin II receptor blockade on renal outcomes in the Irbesartan Diabetic Nephropathy Trial: clinical implications and limitations. *J Am Soc Nephrol* 2005 Oct;16(10):3027-37. Epub 2005 Aug 24

10. Patel A, MacMahon S, Chalmers J, Neal B, Woodward M, Billot L, Harrap S, Poulter N, Marre M, Cooper M, Glasziou P, Grobbee DE, Hamet P, Heller S, Liu LS, Mancia G, Mogensen CE, Pan CY, Rodgers A, Williams B. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet*. 2007 Sep 8;370(9590):829-40.

11. Barnett AH, Bain SC, Bouter P, Karlberg B, Madsbad S, Jervell J, Mustonen J. Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy. *N Engl J Med* 2004 Nov 4;351(19):1952-61. Epub 2004 Oct 31.

12. Hansen HP, Tauber-Lassen E, Jensen BR, Parving HH. Effect of dietary protein restriction on prognosis in patients with diabetic nephropathy. *Kidney Int* 2002 Jul;62(1):220-8.

13. Bakris GL, Copley JB, Vicknair N, Sadler R, Leurgans S. Calcium channel blockers versus other antihypertensive therapies on progression of NIDDM-associated nephropathy. *Kidney Int* 1996 Nov;50(5):1641-50.

14. Standards of Medical Care in Diabetes—2012. *Diabetes Care*, 2012 vol 35 Supplement 1 S11-S61.

15. Levinsky NG. Specialist evaluation in chronic kidney disease: too little, too late. *Ann Intern Med* 2002; 137: 542-543.

16. Lewis EJ, Hunsicker LG, Bain, BP, Rohde, RD. The effect of angiotensin-converting enzyme inhibition on diabetic nephropathy. *NEJM* 1993; 329: 1456-1462.

17. Laffel, LM, McGill, JB, Gans DJ. The beneficial effect of angiotensin-converting enzyme inhibition with captopril on diabetic nephropathy in normotensive IDDM patients with microalbuminuria. North American Microalbuminuria Study Group. *Am J Med* 1995; 99: 497-504.

18. Bakris, GL, Williams, M, Dworkin, L, Elliot, WJ, Epstein, M, Toto, R, Tuttle, K, Douglas, J, Hsueh, W, Sowers, J. National Kidney Foundation Hypertension and Diabetes Executive Committees Working Group. Preserving renal function in adults with hypertension and diabetes: a consensus approach. *Am J Kidney Dis* 2000: 36: 646-661.

19. Lewis EJ, Hunsicker LG, Clarke WB, Berl T, Pohl MA, Lewis JB, Ritz E, Atkins RC, Rohde R, Raz I. Collaborative Study Group. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *NEJM* 2001: 345: 851-860.

20. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving JJ, Remuzzi G, Snapinn SM, Zhang Z, Shahinfar, S. RENAAL Study Investigators. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *NEJM* 2001: 345: 861-869.

21. Parving, HH, Lehnert, H, Brochner-Mortensen, J, Gomis, R, Anderson, S, Arner, P. Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study Group. The effect of irbesartan on the development of diabetes nephropathy in patients with type 2 diabetes. *NEJM* 2001; 345: 870-878.

22. Viberti, G, Mogensen, CE, Groop, LC, Pauls, JF. Effect of captopril on progression to clinical proteinuria in patients with insulin dependent diabetes mellitus and microalbuminuria. European Microalbuminuria Captopril Study Group. *JAMA* 271, 275-279, 1994.

Retinopathy and Diabetic Eye Disease

Diabetes is the leading cause of blindness in the United States for adults ages 20-74. Many of the early signs of diabetic retinopathy (notable on a dilated fundus examination) are asymptomatic for the patient. Risk factors include chronic hyperglycemia, nephropathy, and hypertension. Intensive glycemic control, control of hypertension, and early diagnosis and treatment of retinopathy may help prevent blindness. The ACCORD Study recently found that the addition of fenofibrate to simvastatin therapy reduced the development and progression of diabetic retinopathy by 37%. There is also new clinical trial evidence that ACE inhibitors and ARBs may prevent the development and slow the progression of mild to moderate non-proliferative retinopathy independent of blood pressure lowering. Screening with high quality fundus photographs may be done and interpreted by a trained eye care provider. However, screening is not a substitute for a comprehensive dilated eye exam, which remains the gold standard for detecting diabetic retinal disease.

The American Diabetes Association recommends an initial, and thereafter an annual, dilated and comprehensive eye exam by an ophthalmologist or optometrist who is knowledgeable and experienced in the diagnosis and management of diabetic retinopathy (see Appendix F). Less frequent exams (2-year intervals) may be considered with the advice of an eye care professional for individual patients in good control and a normal exam. Patients with diagnosed diabetic retinopathy and patients with diabetes with prior normal eye exams who are, or become, pregnant should promptly be referred to an ophthalmologist.

Recommended Eye Examination Schedule for Type 1 and Type 2 Diabetes	
Type of Patient	**Minimum Routine Follow-up**
Type 1 patients (adults and children 10 years and older) should have a dilated eye exam by an optometrist or ophthalmologist within five years after diagnosis. (Some evidence suggests that microvascular complications may develop before age 10 among those diagnosed as infants and toddlers.) **Type 2** patients should have a dilated eye exam shortly following diagnosis of diabetes.	**Do annually for most patients** with non-proliferative diabetic retinopathy (NPDR) or microaneurysms. **Do biennially for patients in good control**, prior normal exam and with advice of an eye care professional. **Do more frequent examination** is required if NPDR is progressing.
Pregnancy: Women should have a dilated eye exam when planning pregnancy if possible, and also during the first trimester. (Does not apply to women with gestational diabetes since they are not at increased risk for diabetic retinopathy.)	**First trimester**, with continued close follow-up and for one year postpartum. Patients with diabetes who become pregnant may experience accelerated diabetic retinopathy and should be monitored closely by an ophthalmologist.
Patients with any type of macular edema, severe non-proliferative diabetic retinopathy (NPDR), or any proliferative diabetic retinopathy (PDR)	**Refer promptly** to an ophthalmologist experienced in the treatment of diabetic retinopathy.*
Patients with vision loss from diabetes should be encouraged to pursue visual rehabilitation.	**Refer** to an ophthalmologist or an optometrist who is trained or experienced in low-vision care.
*Do not delay referral to an ophthalmologist until PDR develops. Early referral is very important for patients with type 2 diabetes and severe NPDR, since laser photocoagulation at this stage is associated with a 50% reduction in risk of severe visual loss and vitrectomy. Source: ADA Clinical Practice Recommendations, *Diabetes Care* 2011;34 (Suppl 1).	

Depression and Diabetes

Depression is twice as common in people with diabetes as in the general population, and rates are higher in women, patients with co-morbid diagnoses, and people who have had the disease for a longer period of time (1). Prevalence varies depending on the methodology and criteria applied, but ranges from 8 to 27% (1, 2, 3, 4).

Patients with depression undiagnosed and/or untreated have poorer control of their disease (especially glycemic control), less adherence to medication and self-testing of blood glucose, and more missed appointments (5, 6). Patients with major depression have a 2-fold increase in incidence of diabetic foot ulcers (7, 8). A diagnosis of diabetes with co-morbid depression also accounts for a higher utilization of health care resources than diabetes without depression (6) and, in the Nurses' Health Study of 78,000 US women, dual diagnoses of depression and diabetes age-adjusted mortality risks were 3.11 vs 1.76 for depression alone and 1.71 for diabetes alone (9).

A practice of routine screening for depression may uncover undiagnosed depression, and therapy may aid in improved diabetes control and will likely improve the quality of life in persons with diabetes (12). The PHQ-9 has been validated in persons with diabetes (10); screening for psychosocial problems including depression, anxiety, diabetes distress, eating disorders, and cognitive impairment is recommended by the ADA when self-management is poor (13).

Adult patients with a diagnosis of diabetes should be screened for depression using any screening method that the provider prefers [e.g., Zung Self-Assessment Depression Scale, Beck Depression Inventory, the Center for Epidemiologic Study Depression Scale (CES-D)], or by asking the following two screening questions:

1. **"Over the past 2 weeks have you felt down, depressed, or hopeless?"**
2. **"Over the past 2 weeks have you felt little interest or pleasure in doing things?"** (11)

The choice of screening method will vary depending on the population served and the practice setting.

All positive screenings should trigger a full history and examination using standard diagnostic criteria to determine the presence or absence of a specific depressive disorder.

Intervention, as needed, may include pharmacotherapy, psychotherapy, collaborative care models (12), and/or other interventions as appropriate.

Resources for Screening and Diagnostic Methods

PHQ: www.depression primarycare.org/clinicians/toolkits/materials/forms/phq9/

Zung: www.mentalhealthministries.net/links_resources/flyers/zung_scale.pdf

Beck: www. psychcorp.pearsonassessments.com/pai/ca/cahome.htm

CES-D: www.depression-help-resource.com/cesd-depression-test.pdf

References

1. Ali S, Stone MA, Peters JL, Davies MJ, Khunti K. The prevalence of co-morbid depression in adults with Type 2 diabetes: a systematic review and meta-analysis. *Diabet Med*. 2006 Nov;23(11):1165-73.

2. Pouwer F, Beekman AT, Nijpels G, Dekker JM, Snoek FJ, Kostense PJ, Heine RJ, Deeg DJ. Rates and risks for co-morbid depression in patients with Type 2 diabetes mellitus: results from a community-based study. *Diabetologia*. 2003 Jul;46(7):892-8. Epub 2003 Jun 18.

3. Collins MM, Corcoran P, Perry IJ. Anxiety and depression symptoms in patients with diabetes.*Diabet Med*. 2009 Feb;26(2):153-61.

4. Osborn CY, Patel KA, Liu J, Trott HW, Buchowski MS, Hargreaves MK, Blot WJ, Cohen SS, Schlundt DG. Diabetes and Co-morbid Depression Among Racially Diverse, Low-Income Adults. *Ann Behav Med*. 2010 Nov 23.

5. Gonzalez JS, Safren SA, Cagliero E, Wexler DJ, Delahanty L, Wittenberg E, Blais MA, Meigs JB, Grant RW. Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. *Diabetes Care*. 2007 Sep;30(9):2222-7.

6. Paul S. Ciechanowski, MD, MPH; Wayne J. Katon, MD; Joan E. Russo, PhD. Impact of Depressive Symptoms on Adherence, Function, and Costs *Arch Intern Med*. 2000;160:3278-3285.

7. Williams LH, Miller DR, Fincke G, Lafrance JP, Etzioni R, Maynard C, Raugi GJ, Reiber GE. Depression and incident lower limb amputations in veterans with diabetes. *J Diabetes Complications*. 2010 Aug 26.

8. Williams LH, Rutter CM, Katon WJ, Reiber GE, Ciechanowski P, Heckbert SR, Lin EH, Ludman EJ, Oliver MM, Young BA, Von Korff M. Depression and incident diabetic foot ulcers: a prospective cohort study. *Am J Med*. 2010 Aug;123(8):748-754.e3.

9. Pan A, Lucas M, Sun Q, van Dam RM, Franco OH, Willett WC, Manson JE, Rexrode KM, Ascherio A, Hu FB. Increased mortality risk in women with depression and diabetes mellitus. *Arch Gen Psychiatry*. 2011 Jan;68(1):42-50.

10. van Steenbergen-Weijenburg KM, de Vroege L, Ploeger RR, Brals JW, Vloedbeld MG, Veneman TF, Hakkaart-van Roijen L, Rutten FF, Beekman AT, van der Feltz-Cornelis CM. Validation of the PHQ-9 as a screening instrument for depression in diabetes patients in specialized outpatient BMC *Health Serv Res*. 2010 Aug 12;10:235.

11. *Guide to Clinical Preventive Services* 2005, Screening for Depression, PP. 98-101.

12. Katon WJ, Von Korff M, Lin EH, Simon G, Ludman E, Russo J, Ciechanowski P, Walker E, Bush T. The Pathways Study: a randomized trial of collaborative care in patients with diabetes and depression. *Arch Gen Psychiatry*. 2004 Oct;61(10):1042-9.

13. ADA *Diabetes Care*. 2011 Jan;34(suppl 1).

Vaccine Administration in Adults with Diabetes

Pneumococcal Vaccine
Pneumococcal Polysaccharide (PPSV)

1. Vaccinate all people with diabetes 2-64 years of age.

2. A one-time revaccination is indicated for:
   - All adults age 65 years and older who were previously vaccinated with PPSV prior to age 65 years if 5 years (or more) have elapsed since the previous dose;

   - All adults who are at highest risk of serious pneumococcal disease or are likely to have a rapid decline in pneumococcal antibody levels if 5 years (or more) have elapsed since the previous dose.

   Highest risk conditions include immune-compromised persons, including those with HIV infection, leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy, chronic renal failure (including dialysis patients), or nephrotic syndrome; those receiving immunosuppressive therapy (including long-term systemic corticosteroids); and those who have received an organ or bone marrow transplant.

Source
ACIP technical content reviewed by the Centers for Disease Control and Prevention, September 2009.

Influenza Vaccine
Seasonal and H1N1

CDC recommends that inactivated seasonal influenza vaccine be administered to all adults with diabetes as soon as it becomes available yearly.

Source
http://www.cdc.gov/mmwr/PDF/wk/mm5901-Immunization.pdf

Appendices

Diabetes Self-management Education

Diabetes self-management education (DSME, sometimes called diabetes self-management training or DSMT) consists of education from a multidisciplinary team of health care professionals. An individualized program is developed to meet patient needs. Instruction may cover any or all of the following topics:

- The diabetes disease process and treatment options
- Incorporating nutritional management into lifestyle
- Incorporating physical activity into lifestyle
- Using medications safely and for maximum therapeutic effectiveness
- Monitoring blood glucose and other parameters, and interpreting/using the results for self-management decision making
- Preventing, detecting, and treating acute complications
- Preventing, detecting, and treating chronic complications
- Developing personal strategies to address psychosocial issues and concerns
- Developing personal strategies to promote health and behavior change
- Promoting preconception care, management of pregnancy, and gestational diabetes

For reimbursement, most health insurance plans require DSME programs to be recognized by ADA or AADE, or certified by the Utah Diabetes Prevention and Control Program (DPCP). Check with health plans to assure eligibility for reimbursement.

NOTE: Medicare reimburses only for DSME provided by approved programs. Prior authorization is required.

State-certified Programs (current as of October 2012)		
Program	City	Phone
Lakeview Hospital	Bountiful	801-299-2470
Brigham City Hospital	Brigham City	435-734-4339
Journey into Wellness, Ute Tribe-Uintah & Ouray Service Unit	Fort Duchesne	435-725-6890
Moab Regional Hospital	Moab	435-259-7191
Mountain View Hospital	Payson	801-465-7045
Castleview Hospital	Price	435-636-4822
Sevier Valley Hospital	Richfield	435-893-0371
Primary Children's Hospital	Salt Lake City	801-588-2729
St. Mark's Hospital	Salt Lake City	801-268-7358
Santaquin Pharmacy	Santaquin	801-754-1141
Jordan Valley Medical Center	West Jordan	801-562-4245
Granger Professional Pharmacy	West Valley	801-965-3639

ADA-recognized Programs can be found online: http://professional.diabetes.org/ERP_List.aspx Insert your zip code or select your state to view all programs.

AADE-recognized Programs can be found online: http://www.diabeteseducator.org/ProfessionalResources/accred/Programs.html#Utah
To find an AADE-Certified Diabetes Educator: http://www.diabeteseducator.org/DiabetesEducation/Find.html

In addition to the programs listed above, there are a few unaccredited DSME programs in Utah. All Utah Community Health Centers participate in a National Diabetes Collaborative; their staff have received training in diabetes treatment and education.

Visit www.auch.org for more information.

Using the 1700 Rule
for Type 1 Physiologic Insulin

The 1700 Rule can be used to guide the patient's dosage of insulin in two circumstances:
- To determine a correction dose for a high PG reading
- To calculate insulin-to-carbohydrate ratio (i.e., to anticipate insulin needed to cover the carbohydrate content of a meal)

To calculate either circumstance:

1. Determine the current total daily dose (TDD): Add up total insulin dose the patient takes in a 24-hour period (rapid + long-acting).
2. Divide 1700 by the TDD. This is the predicted amount (mg/dL) the PG will lower for every 1 unit of rapid acting insulin added.
3. Increase rapid-acting insulin by the number of units needed to reduce the PG to an appropriate level (<140 mg/dL).
4. Encourage the patient to keep careful records of resulting PG readings. (Most helpful readings are FPG, 1-2 hour PPG, and bedtime PG).

Example*

Patient takes 50 units of insulin/day

(TDD = 50)
5. 1700/50 = 34 (Round to a convenient number like 35, which means 1 unit of insulin will lower PG by ~35 points)
6. So, if PG is 175, use 1 extra unit to drop it to 140. If PG is 210, use 2 extra units, etc.,
7. Or, 1 Unit per 30-50 mg/dL. (If HS correction used, ↓ to 50% of usual dose.)

*A more exact method of insulin dose calculation has been published, but the method presented here provides a simple approximation. Exact method reference: Davidson, PC, Hebblewhite, HR, Steed, RD, Bode, BW. *Endocr Pract* 14:1095-1101 (2008).

To calculate insulin-to-carb ratio:

1. Determine the current total daily dose (TDD): Add up ALL the insulin the patient takes in a 24-hour period (rapid + long-acting)
2. Divide 1700 by the TDD. This is the predicted amount (mg/dL) the PG will lower for every 1 unit of rapid-acting insulin added.
3. Multiply predicted PG lowering (mg/dL) x .33 This is the number of grams of carbohydrate covered by 1 unit of insulin. (For most people, a starting dose would be 1 unit of rapid-acting insulin for every 10-15 grams of carbohydrate to be eaten.)

Example

1. Patient takes 50 units of insulin/day (TDD = 50)
2. 1700/50 = 34 (round to 35, which means 1 unit of insulin lowers BG by ~35 points)
3. 35 X .33 = 11-12 (which means patient will need 1 unit of insulin for every 11-12 grams of carbohydrate anticipated in a meal)

Medications

Class	Drug Generic Name	Dispensed As	Cost/ mo*	Dosage Regimen
Alpha Glucosidase Inhibitors	Acarbose	Generic: 25 mg 50 mg 100 mg	$43 $49 $98	150-300 mg/day in three divided doses
		Precose: 25 mg 50 mg 100 mg	$100 $110 $129	
	Miglitol	Glyset: 25 mg 50 mg 100 mg	$100 $110 $129	150-300 mg/day in three divided doses
Biguanides	Metformin (immediate-release)	Generic: 500 mg 850 mg 1000 mg	$3 $4 $4	1000-2550 mg/day in 2-3 divided doses
		Glucophage: 500 mg 850 mg 1000 mg	$68 $115 $139	
	Metformin (extended-release)	Generic: 500 mg 750 mg	$2 $4	500-2000 mg/day, given as a single dose or in two divided doses.
		Glucophage XR: 500 mg 750 mg	$35 $52	
Dipeptidyl Peptidase IV (DPP-4) Inhibitors	Sitagliptin	Januvia: 25 mg 50 mg 100 mg	$227 $227 $227	25-100 mg/day as a single dose
	Saxagliptin	Onglyza: 2.5 mg 5.0 mg	$221 $221	2.5-5.0mg/day as a single dose
	Linagliptin	Tradjenta: 5 mg	Prices not available	5 mg once daily
Meglitinides	Nateglinide	Starlix: 60 mg 120 mg	$199 $204	180 mg-360 mg/day in three divided doses
	Repaglinide	Prandin: 0.5 mg 1 mg 2 mg	$210 $210 $210	1-16 mg/day in two to four divided doses
Thiazolidinedione (TZD)	Pioglitazone	Actos: 5 mg 30 mg 45 mg Now available generic	$174 $265 $288	15-45 mg once daily

*per January 2011 AWP or MAC, where available

Medications

Class	Drug Generic Name	Dispensed As	Cost/ mo*	Dosage Regimen
Sulfonylureas	Glimepiride	Generic: 1 mg 2 mg 4 mg	$2 $3 $3	1-4 mg/day as a single dose
		Amaryl: 1 mg 2 mg 4 mg	Prices not available	
	Glipizide (extended-release)	Generic: 2.5 mg 5 mg 10 mg	$7 $5 $8	5-20 mg/day as a single dose
		Glucotrol XL: 2.5 mg 5 mg 10 mg	Prices not available	
	Glipizide (immediate-release)	Generic: 5 mg 10 mg	$2 $2	5-40 mg/day given as a single dose or in two divided doses
		Glucotrol: 5 mg 10 mg	$22 $39	
	Glyburide (conventional tab)	Generic: 1.25 mg 2.5 mg 5 mg	$6 $7 $8	1.25-20 mg/day, given as a single dose or in two divided doses
		Diabeta: 1.25 mg 2.5 mg 5 mg	$11 $22 $40	**Note:** Least preferred for side effects of recurrent hypoglycemia and risk of coronary side effects
		Micronase: 1.25 mg 2.5 mg 5 mg	Prices not available	
	Glyburide (micronized tablet)	Generic: 1.5 mg 3 mg 6 mg	- $2 $3	0.75-12 mg/day, given as a single dose or in two divided doses
		Glynase Prestab: 1.5 mg 3 mg 6 mg	$27 $45 $71	
Injectable	Exenatide	Byetta: 5 mcg 10 mcg	$378	Twice daily
	Exenatide ER	Bydureon: 2 mg	$378	Inject 2 mg once weekly
	Liraglutide	Victoza: 0.6mg 1.2mg 1.8mg	$364	Once daily (18 mg/3 mL pen)
	Pramlintide	Symlin: 60 inj. Pen (1.5 mL) 120 inj. Pen (3 mL)	$280	Dose type 2: 60-120 mcg daily Dose type 1: 15-60 mcg daily

*per January 2011 AWP or MAC, where available

Class	Drug Generic Name	Dispensed As	Cost/ mo*	Dosage Regimen
Combination Oral Medications	Glipizide/ Metformin	Generic: 2.5 mg-500 mg	$19	Daily dose ranges from Glipizide 2.5 mg/Metformin 500 mg to Glipizide 20 mg/Metformin 2000 mg; given in 1-2 divided doses with meals
		Metaglip: 2.5 mg-250 mg	$34	
	Glyburide/ Metformin	Generic: 1.25 mg/250 mg 2.5 mg/500 mg 5 mg/500 mg	$7 $7 $7	Daily dose ranges from Glyburide 1.25 mg/Metformin 250 mg to Glyburide 20 mg/Metformin 2000 mg; given in 1-2 divided doses with meals. Glucovance twice daily
		Glucovance: 1.25 mg-250 mg 2.5 mg-500 mg 5 mg-500 mg	$89 $89 $89	
	Linagliptin/ Metformin	Jentadueto: 2.5 mg/500 mg 2.5 mg/850 mg 2.5 mg/1000 mg	Prices not available	1 tablet twice daily; maximum dose is 5 mg/ 2000 mg daily
	Pioglitazone/ Glimepiride	Duetact: 30 mg/2 mg 30 mg/4 mg	$265 $265	Daily dose ranges from Pioglitazone 30 mg/Glimepiride 2 mg to Pioglitazone 45 mg/Glimepiride 8 mg; given once daily
	Pioglitazone/ Metformin	Actoplus Met: 15/500 mg 15/850 mg	$264	Daily dose ranges from 15 mg/500 mg to 45 mg/2550 mg; given in up to three divided doses with meals
	Pioglitazone/ Metformin XR	Actoplus Met XR: 15/1000 mg 30/1000 mg	$143 $283	15 mg/1000 mg to 30 mg/1000 mg; once daily
	Saxagliptin/ Metformin XR	Kombiglyze XR: 5mg/500mg 2.5mg/1000mg 5.0mg/1000mg	$221 $221 $111	2.5/1000 to 5.0/2000; once daily
	Sitagliptin/ Metfomin	Janumet: 50 mg/500 mg 50 mg/1000 mg	$227 $227	Daily dose ranges from 100 mg/1000 mg to 100 mg/2000 mg; given in two divided doses with meals.
	Sitagliptin/ Metformin XR	Janumet XR: 50 mg/500 mg 50 mg/1000 mg 100 mg/1000mg	Prices not available	1 or 2 tablests daily; maximum dose is 100 mg/2000 mg daily

*per January 2011 AWP or MAC, where available

Comprehensive Foot Examination

HISTORY

Yes	No	
☐	☐	Prior amputation
☐	☐	Prior ulcer
☐	☐	Claudication
☐	☐	Paresthesia
☐	☐	Can reach feet
☐	☐	Can see feet
☐	☐	Prior education
☐	☐	Extensive walking
☐	☐	Insoles for shoes
☐	☐	Special shoes

Right Foot   **Left Foot**

PEDAL PULSES   ⊕ = sensate ⊖ = insensate

	R	L
DP	_____	_____
PT	_____	_____

SKIN ABNORMALITIES
☐ None
☐ Some – see diagram

C=callus	D=dryness
PU=pre-ulcer	E=erythema
F=fissure	W=warmth
M=maceration	S=swelling
U=ulcer	

NAIL ABNORMALITIES
☐ None
☐ Some:

	R	L
Hemorrhage	☐	☐
Ingrown	☐	☐
Fungus	☐	☐
↑↑Length	☐	☐

SHOE EXAM

Inappropriate style?	☐ Yes	☐ No
Lean to one side?	☐ Yes	☐ No
Flattened insole?	☐ Yes	☐ No
Inadequate fit?	☐ Yes	☐ No

10 G MF TESTING   ⊕ = sensate ⊖= insensate
☐ Sensate   ☐ Insensate

VIBRATION TESTING
☐ Normal   ☐ Abnormal

ANKLE REFLEXES
☐ Normal   ☐ Absent

PIN PRICK SENSED
☐ Yes   ☐ No

DEFORMITIES
☐ None
☐ Some:

	R	L
Hammertoes	☐	☐
Claw toes	☐	☐
Prom. MT heads	☐	☐
Bunion, 1st MTP	☐	☐
Bunion, 5th MTP	☐	☐
Collapsed arch	☐	☐
Limited Joint Mobility		
1st MTP (<50° DF)	☐	☐
Ankle (<100° DF)	☐	☐

☐ Amputation: Level =

CKD Assessment Algorithm

Patient Office Visit

Is patient at risk for CKD?

Susceptibility
–Age > 60 years
–Family history of CKD

Direct Risk Factors
–Diabetes
–High blood pressure
–Autoimmune diseases
–Lower urine tract obstruction
–Hx acute renal failure

–Systemic infections
–Urinary tract infection
–Urinary stones
–Drug toxicity
–Exposure drugs/contrast

Progressive Risk Factors
–High levels proteinuria
–Malignant hypertension
–Poor glycemic control
–Smoking

No → **STOP**

Yes

Perform routine screening for CKD for patients at increased risk

–Serum creatnine to determine estimated eGFR   –Assessment of proteinuria   –Urinalysis for presence of white & red blood cells

Yes ← Does patient have abnormal eGFR > 3 months? → No → Does patient have protein to creatinine ratio > 1.0 mg/mg? → No

Determine Stage of CKD

Yes

Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
eGFR > 90 P:C > 1.0 x 2	eGFR 60-89	eGFR 30-59	eGFR 15-29	eGFR < 15

Follow Up CKD Monitoring
–Test patients at risk for CKD annually
–Counsel patients at risk for CKD but found not to have CKD to reduce risk factors when possible

Begin CKD Treatment: Develop Clinical Action Plan

Collaborate with nephrologist to develop action plan to include:
–Evaluate and manage comorbid conditions (Primary care, all stages)
–Slow the loss of kidney function (Co-management, all stages)
–Prevent & treat cardiovascular disease (Primary care, all stages)
–Prevent & treat complications of decreased kidney function (Co-management, all stages)
–Prepare for kidney failure and replacement therapy (Nephrology, stage 4)
–Replace kidney function (Nephrology, stage 5)

Consult nephrologist if action plan cannot be performed or carried out or eGFR < 60

Identify risks associated with CKD

–Evaluate etiology of kidney disease
–Evaluate complications of kidney disease: anemia, hypertension, malnutrition, bone disease, metabolic acidosis, congestive heart failure, hyperkalemia, edema determined to fluid overload, neuropathy
–Evaluate risk for loss of kidney function
–Evaluate comorbid conditions
–Evaluate risk for cardiovascular disease

Assess barriers to treatment adherence

–Family and social support
–Depression
–Income & unemployment concerns
–Stress and coping mechanisms
–Perceptions of illness & treatment
–Limited access to medications and/or care

Review medication usage at follow-up visits

–Evaluate for necessary dose adjustments based on level of kidney function
–Evaluate for adverse effects of medications on kidney function (NSAIDs, IV contrast)
–Evaluate for drug interactions
–Counsel patient to avoid nephrotoxic drugs and IV contrast
–Evaluate appropriateness for ARB/ACE inhibitor with diagnosis of HTN/diabetes
–Evaluate need for therapeutic drug monitoring

Monitor CKD Progression ← No ← Does patient have eGFR < 60 for > 3 months or proteinuria > 3 gm? → Yes →

Consult/Refer to Nephrologist

–Consult nephrologist at Stage 1 if hematuria or significant proteinuria present
–Consult nephrologist at Stage 2 if eGFR declines > 4mL/min/yr
–Consult nephrologist at Stage 3 for all patients with CKD
–Refer patient to nephrologist for evaluation when eGFR < 30 mL/min/1.73^2

CKD Treatment Algorithm

CKD Treatment Algorithm

CKD Stage 1
eGFR > 90
mL/min/1.73 m^2
P:C ratio > 1.0 mg/mg
creatinine x 2

PRIMARY CARE
Assess Complications

LABS
- BP monitoring q 6 mo.
- eGFR q 12 mo.
- Urinalysis q 12 mo. to assess hematuria, proteinuria, microalbuminuria
- Lipids q 12 mo.
- If diabetic, Hgb A$_1$C and microalbuminuria q 12 mo.

RISK ASSESSMENT
- Avoidance of nephrotoxic agents & dyes
- Immunizations
  - Flu vaccine q 12 mo.
  - Pneumovax, as indicated
  - Hep B vaccine, as indicated
- Assess cardiovascular risk:
  - Smoking cessation
  - Physical activity

EDUCATION
- Cardiovascular risk
- Medications to avoid
- Immunizations

CKD Stage 2
eGFR 60 - 89
mL/min/1.73 m^2

PRIMARY CARE
Assess Complications

LABS
- BP monitoring q 3-12 mo.
- eGFR q 12 mo.
- Urinalysis q 3 -12 mo. to assess hematuria, proteinuria, microalbuminuria
- Lipids q 12 mo.
- If diabetic, Hgb A$_1$C and microalbuminuria q 12 mo.
- Hgb q 12 mo. if > 11 gm/dL

RISK ASSESSMENT
- Avoidance of nephrotoxic agents & dyes
- Immunizations
  - Flu vaccine q 12 mo.
  - Pneumovax, as indicated
  - Hep B vaccine, as indicated
- Assess cardiovascular risk:
  - Smoking cessation
  - Physical activity

EDUCATION
- Cardiovascular risk
- Medications to avoid
- Immunizations

CKD Stage 3
eGFR 30 - 59
mL/min/1.73 m^2

CO-MANAGEMENT
Assess Complications

LABS
- BP monitoring q 3-12 mo.
- eGFR q 3-12 mo.
- Urinalysis q 6-12 mo. to assess hematuria, proteinuria, microalbuminuria
- Lipids q 12 mo.
- If diabetic, Hgb A$_1$C and microalbuminuria q 12 mo.
- Hgb > 11 q 3-6 mo.
- Hgb < 11 q 1-3 mo.
- Lytes and glucose q 12 mo.
- PTH, Ca & P q 3-12 mo.
- Measure 25(OH)D

RISK ASSESSMENT
- Avoidance of nephrotoxic agents & dyes
- Immunizations
  - Flu vaccine q 12 mo.
  - Pneumovax, as indicated
  - Hep B vaccine, as indicated
- Assess cardiovascular risk:
  - Smoking cessation
  - Physical activity

EDUCATION
- Cardiovascular risk
- Medications to avoid
- Immunizations
- Nutrition: Advise diet low in salt & potassium
- Renal bone disease

CKD Stage 4
eGFR 15 - 29
mL/min/1.73 m^2

NEPHROLOGY
Assess Complications

LABS
- BP monitoring q 3-6 mo.
- eGFR q 3-6 mo.
- Lipids q 12 mo.
- If diabetic, Hgb A$_1$C and microalbuminuria q 12 mo.
- Hgb q 3-6 mo., monthly if on ESA therapy
- PTH, Ca, P. q 3-6 mo.
- Measure 25(OH)D

RISK ASSESSMENT
- Avoidance of nephrotoxic agents & dyes
- Immunizations
  - Flu vaccine q 12 mo.
  - Pneumovax, as indicated
  - Hep B vaccine, as indicated
- Assess cardiovascular risk:
  - Smoking cessation
  - Physical activity

EDUCATION
- Cardiovascular risk
- Medications to avoid
- Immunizations
- Nutrition: Advise diet low in salt, phos. & potassium
- Renal bone disease
- Anemia
- Vascular access placement
- Modality options

REFERRALS
- Surgeon for vascular access placement
- Transplant center for eval

CKD Stage 5
eGFR < 15
mL/min/1.73 m^2

NEPHROLOGY
Assess Complications

LABS
- eGFR q 1-3 mo.
- Lipids q 12 mo.
- If diabetic, Hgb A$_1$C and microalbuminuria q 12 mo.
- Hgb monthly
- PTH, Ca, P q 1-3 mo.
- Measure 25(OH)D
- HBV titer

RISK ASSESSMENT
- Avoidance of nephrotoxic agents & dyes
- Immunizations
  - Flu vaccine q 12 mo.
  - Pneumovax, as indicated
  - Hep B vaccine, as indicated
- Assess cardiovascular risk:
  - Smoking cessation
  - Physical activity

EDUCATION
- Cardiovascular risk
- Medications to avoid
- Immunizations
- Nutrition: Advise diet low in fluids, salt, phos. & potassium
- Renal bone disease
- Anemia
- Vascular access monitoring
- Modality options
- Evaluation for kidney transplant

REFERRALS
- Surgeon for vascular access intervention, as needed
- Transplant center for eval

Adapted with permission from the Renal Network of the Upper Midwest, Inc.

The Kidney Disease Outcomes Quality Initiative (KDOQI) recommendations for Chronic Kidney Disease: Evaluation, Classification, and Stratification were used to develop portions of these documents.

UPPER MIDWEST FISTULA FIRST COALITION

Report of Diabetic Eye Exam

Eye Care Provider	Primary Care Provider
Name:	Name:
Clinic:	Clinic:
Address:	Address:
Phone:	Phone:
Fax:	Fax:
Attention:	Attention:

Date of exam _____ 20____

Dear Dr. _____. I completed a retinal eye examination on the above date for _____(date of birth_____) a patient you have treated for diabetes. The information below is a summary of my findings and report. I recommend that this patient be rechecked in _____ months.

Retinal eye exam summary

☐ Eyes were dilated for this exam

☐ No diabetic retinopathy

☐ Diabetic retinopathy requiring no treatment at this time

☐ Diabetic retinopathy requiring treatment

☐ Other eye disease:

Recommended treatment and follow-up:

If you have any questions, please contact me at the address or telephone number listed above.

Sincerely,

(Signature of Eye Care Provider)

HEALTH
UTAH DEPARTMENT OF
Diabetes Prevention & Control Program

Tobacco Quit Line Referral Form

Utah Tobacco Quit Line
1.800.Quit.Now
The TRUTH

Utah Tobacco Quit Line
Fax Form
Fax to: 1-800-483-3076

PATIENT INFORMATION (PRINT CLEARLY)

Patient name (Last) _____, (First) _____

Date of birth _____
Gender ☐ M ☐ F

Address _____ City _____, State UT Zip code _____

Phone #1 (____) ____-____ #2 (____) ____-____ Email _____

Cell Phone # (____) ____-____ Text Message ☐ Yes ☐ No

Best times to call ☐ morning ☐ afternoon ☐ evening Weekends ☐ Yes ☐ No

May we leave a message? ☐ Yes ☐ No

Language ☐ English ☐ Spanish; other _____ Are you hearing impaired and need assistance? ☐ Yes ☐ No

_____ I am ready to quit tobacco and request that the Utah Tobacco Quit Line contact me to help with my quit plans.

I understand that the Utah Tobacco Quit Line will inform my provider about the services and cessation medications provided to me.

Patient signature _____ Date _____

This release shall be valid for one year after the above date.

PROVIDER INFORMATION (PRINT CLEARLY)

Clinic/Hosp/Dept _____   contact name _____

Address _____   E-mail (optional) _____

city/state/zip _____   Phone (____) ____-____

Fax (____) ____-____

PLEASE COMPLETE FORM AND FAX OR MAIL TO:

FAX 1-800-483-3076
Utah Tobacco Quit Line
National Jewish Health™
1400 Jackson St., M302
**Denver, CO 80206**

Healthy Eating with Diabetes

While there is no such thing as a "diabetic diet," but people with diabetes need to be especially careful about what they eat. There are many eating plans available, but the best one is the one that fits your medications, lifestyle, and needs. One of the most important things you can do to eat healthy and control your diabetes is to meet with a Registered Dietitian and/or Certified Diabetes Educator who can help you learn to make good food choices. Most insurance plans cover this.

Tips for Healthy Eating:

- Choose fresh fruits and vegetables most often

- Avoid sugary drinks like soda, punches, sports drinks, and juice

- Be aware of portion sizes!

  - A serving of carbohydrate is a half-cup or about the size of a tennis ball. Depending on your personal needs, you may have 2-5 such portions at each meal or for a snack. A dietitian or diabetes educator can help you find out how many carbohydrate servings you need.

  - A serving of meat for the main meal is the size of a deck of cards. You may want to have a portion this size with your main meal of the day. Having less at other meals may be better for you.

Here are some eating plans that may help you.

MyPlate: The online program at ChooseMyPlate.gov can help you create a personal nutrition plan, set your goals, and track your progress. ChooseMyPlate.gov includes tools to track your physical activity, too. Use the tools on this website to learn how to read labels. You can also get daily healthy-eating tips. There is even a BMI calculator to help you measure your success.
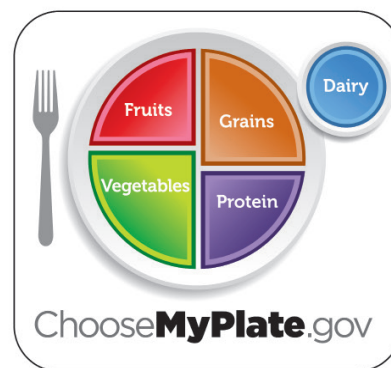
Carbohydrate Counting: Many people with diabetes have successfully controlled their blood sugar by counting carbohydrates (or "carbs"). Carbohydrates are found in most foods. Carbohydrates are often classified as "simple" or "complex." That has to do with how easily your body breaks them down and releases them into your blood. Eating a meal or snack that is high in simple carbs can quickly raise your blood sugar and raise it too high. Carb counting allows you to plan your meals based on the amount and type of carbohydrates you eat so that your blood sugar level is more constant. Keeping your blood sugar level more constant is an important part of controlling your diabetes. Carb counting is easy to do, but can be tricky to learn. The best way to learn this skill is to meet with a Registered Dietitian and/or Certified Diabetes Educator. These online resources may help you:

- http://www.diabetes.org/food-and-fitness/food/planning-meals/
- http://www.dlife.com/diabetes/information/food_and_nutrition/diet_and_carb_counting.html
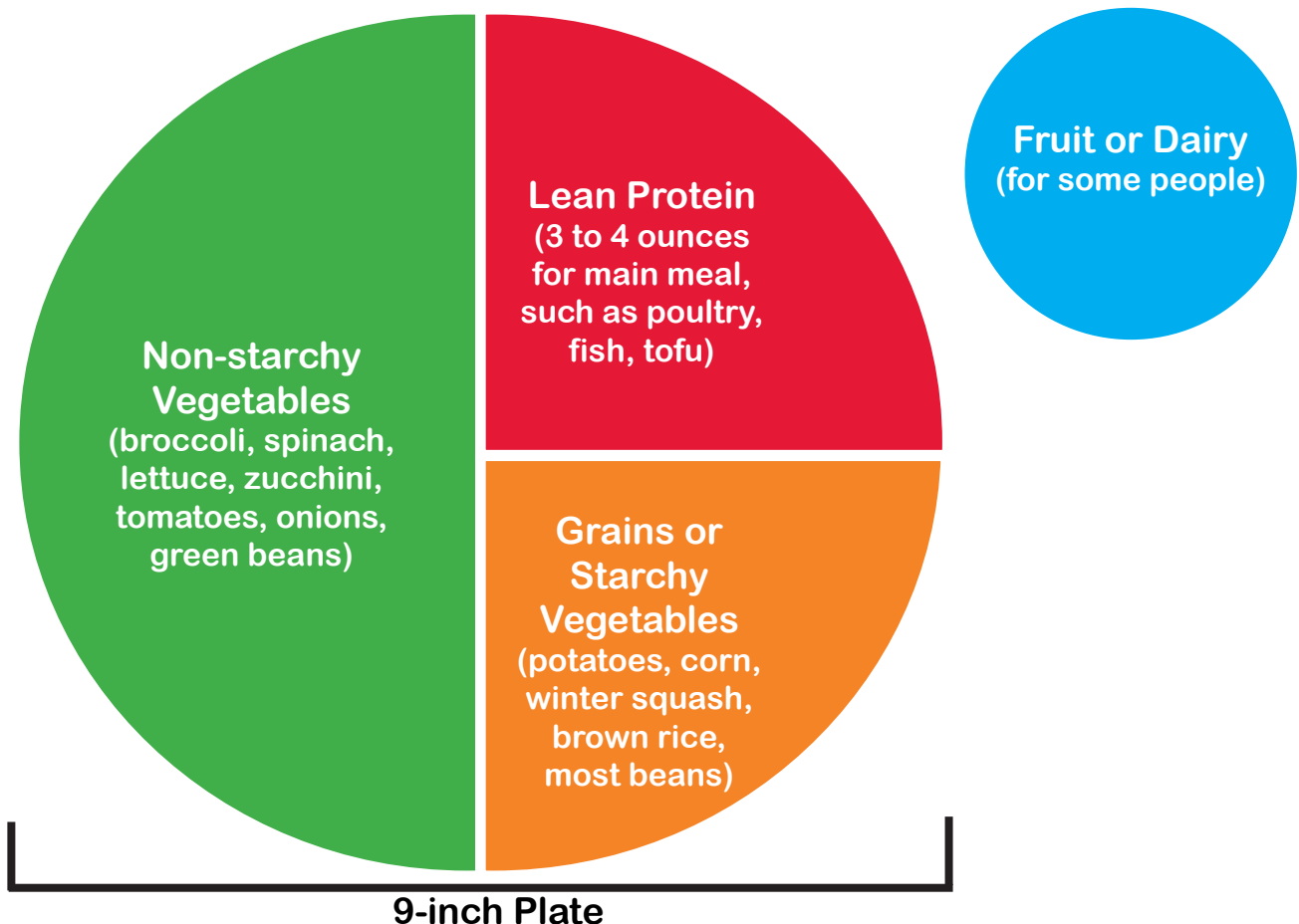
PATIENT EDUCATION

Healthy Eating with Diabetes: Plate Method

The Plate Method shows you about how much you need to eat of different types of food to lose weight and keep carbohydrate amounts and blood sugar constant. Not all dinner plates are the same size! You might want to consider using a smaller plate (9" diameter) to help you control your portions.

Here's what to put on your plate:

- Fill about half of your plate with non-starchy vegetables. There are so many non-starchy vegetables to choose from: broccoli, spinach, lettuce, zucchini, tomatoes, peppers, onions are a few examples. These are very low in calories and carbohydrates. They're also high in important nutrients.

- Fill about one-quarter of your plate with carbohydrates from grains (preferably whole grains) and starchy vegetables. Starchy vegetable such as potatoes, corn, beans (except green beans) and winter squash go on this part of your plate. Fruit and dairy food are also carbohydrates and may go here, see the next note.

- Depending on personal needs, some people will also have a serving of dairy, fruit, or even a small amount of sweets in addition to the carbohydrate portion of the plate.

- Fill the last quarter of your plate with lean protein like seafood, lean beef, tofu, poultry, and eggs. For your main meal, the serving size should be about 3 to 4 ounces. Less or sometimes no meat is usually better for the other meals. This depends on your weight and other factors.

- If you use fats, mainly use healthy fats such as olive, canola, or peanut oil and products made from them. But, only use a little as they are high in calories!

PATIENT EDUCATION

Non-starchy Vegetables
(broccoli, spinach, lettuce, zucchini, tomatoes, onions, green beans)

Lean Protein
(3 to 4 ounces for main meal, such as poultry, fish, tofu)

Grains or Starchy Vegetables
(potatoes, corn, winter squash, brown rice, most beans)

Fruit or Dairy
(for some people)

9-inch Plate

Monitoring Your Blood Glucose

<u>**WHY:**</u> By using a blood glucose monitor and keeping records, you will be able to control your diabetes. The monitor and record help you to identify causes of high levels, as well as the effect of food and exercise on diabetes.

<u>**HOW TO GET A MONITOR:**</u> A monitor may be acquired from your doctor, the pharmacy, or your insurance group. Remember, many insurance companies require a certain brand, so check on this.

<u>**HOW TO USE:**</u> Most monitors work in the same way. Get a small drop of blood, then hold the strip against the drop, and the machine will give a number within a few seconds. Follow these steps:
1. After washing your hands, insert a test strip into your meter.
2. Use your lancing device on the side of your fingertip to get a drop of blood.
3. Gently squeeze or massage your finger until a drop of blood forms. (Required sample sizes vary by meter.)
4. Touch and hold the edge of the test strip to the drop of blood, and wait for the result.
5. Your blood glucose level will appear on the meter's display.
   Note: All meters are slightly different, so always refer to your user's manual.

<u>**WHEN TO TEST:**</u> This depends on your diabetes and your doctor's request.
Type 1: May be as often as 6 times a day
Type 2: May be once a day. (Test before eating one day, followed by two hours after dinner the next day.) May be as often as four times a day, especially when adjusting medications, or evaluating food and activity.
Gestational: Usually fasting, two hours after meals, and at bedtime.

<u>**WHAT ARE THE TYPICAL RANGES?**</u>

These are blood glucose ranges for adults with diabetes:

A1C	<7%
Preprandial (before a meal) plasma glucose	70–130 mg/dL
Postprandial (after a meal) plasma glucose	<140 mg/dL

<u>**EXAMPLE OF BLOOD GLUCOSE LOG**</u>

	Breakfast	Lunch	Dinner	Bedtime	Other	Notes
	Blood Sugar	Blood Sugar	Blood Sugar	Blood Sugar	Blood Sugar	
Mon	108	118	121	112		
Tues	112	109		*151		* Missed evening walk. Start back tomorrow!
Wed	125	122	130	*121		
Thur	114	129	185	*242		* Sick with flu? Drank diet soda. No ketones.
Fri	156	148	135	130		Feeling better today.
Sat	128		125	*151	129 at 11p.m.	* Extra juice made sugar go up.
Sun	120	119	*168	133		* Lunch at church.

Taking Care of Your Feet

- Inspect your feet daily! This may require a mirror, magnifying glass, or the help of another person.
- Call your doctor if you have redness that doesn't go away, a growing callus, or a bleeding callus.
- Test your bath water temperature with your hand, not your foot.
- Wash and dry your feet daily.
- Apply cream or petroleum jelly to your feet every day, but not between your toes.
- Do NOT use a pumice stone or other instrument to file a nail or remove a callus, especially if your vision is bad or you have lost feeling in your feet. See a podiatrist or other health professional.
- If you've lost sensation in your feet, do appropriate exercise.
- Never walk around barefoot or wearing just socks, even when you are at home.
- Always wear optimal footwear—at all times!

Footwear Guidelines

To Keep Your Feet Healthy, Avoid:	Instead, Choose:
Pointed toes	Broad, round toes
Slip-ons	Adjustable (laces, buckles, Velcro)
Open toes/ High heels	Athletic shoes or walking shoes
Plastic	Leather or canvas
Black color	White/light colors
Too small	½" between longest toe and end of the shoe

PATIENT EDUCATION